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(71) Applicant (for all designated States except US): FLORENCE MEDICAL LTD. [IL/IL]; Sharona Center, Derech Hasharon 12, 44269 Kfar-Saba (IL).		
(72) Inventors; and		
(75) Inventors/Applicants (for US only): TOLKOWSKY, Gideon [IL/IL]; Enzio Sireni Street 3, 46735 Herzlia Pituch (IL). DGANY, Elhanan [IL/IL]; Gordon Street 14, 44260 Kfar Saba (IL). SHALMAN, Evgeny [IL/IL]; Adirim Street 5/4, 39088 Tel Aviv (IL). NOSKOWICZ, Simon, Henri [IL/IL]; Herzl Street 22/22, 44444 Kfar Saba (IL). BARAK, Chen [IL/IL]; Bareket Street 18, 73142 Shoham (IL). ORTEN-BERG, Michael [IL/IL]; Hagenev Street 60/2, 40300 Kfar Yona (IL).		
(74) Agent: EITAN, PEARL, LATZER & COHEN-ZEDEK; 2 Gav Yam Center, Shenkar Street 7, 46725 Herzlia (IL).		
(54) Title: APPARATUS AND METHOD FOR IDENTIFICATION AND CHARACTERIZATION OF LESIONS AND THERAPEUTIC SUCCESS BY FLOW DISTURBANCES ANALYSIS		
(57) Abstract		
<p>A medical intratherapeutic diagnostic system (1) includes a signal analyzer (10), and a pressure sensor device (4) adapted for use in the fluid delivery system of a living body, such as a blood vessel system. The system (1) measures flow disturbances found within the blood vessel for the purpose of determining the characteristics of the blood vessel walls including indications of stenosis, aneurism, therapeutic success (balloon dilatation, dissection or stent malposition). The flow disturbance measured is created by the blood flow within areas of atherosclerotic occlusion of blood vessels. The system (1) of the present invention increases the amount of knowledge available to the treating physician about the occlusion size, and blood flow capacity.</p>		

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**APPARATUS AND METHOD FOR IDENTIFICATION AND  
CHARACTERIZATION OF LESIONS AND THERAPEUTIC SUCCESS BY  
FLOW DISTURBANCES ANALYSIS**

**BACKGROUND OF THE INVENTION**

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**FIELD OF INVENTION**

The present invention relates to the field of medical diagnostic devices and therapeutic evaluation in general and to a system for intravascular characterizing blood vessel walls and lesions in particular.

**DESCRIPTION OF THE RELATED ART**

10       Vascular diseases are often manifested by reduced blood flow due to atherosclerotic occlusion of vessels. For example, occlusion of the coronary arteries supplying blood to the heart muscle is a major cause of heart disease. Invasive procedures for relieving arterial blockage such as bypass surgery and balloon dilatation with a catheter are currently performed relying on estimates of the occlusion characteristics and the blood flow through  
15       the occluded artery. These estimates are based on measurements of occlusion size and / or blood flow. Unfortunately, current methods of occlusion size and blood flow measurement have low resolution, are inaccurate, are time consuming, require expertise in the interpretation of the results and are expensive. Thus, decisions on whether or not to use any of the blockage relieving methods and which of the methods should be used are often  
20       based on partial information. The evaluation of therapeutic success is also problematic, where both occlusion opening and stent position have to be evaluated.

25       Pressure, flow and geometry are three variables often measured in the cardiovascular system. Recent progress in probe miniaturization, improvements of the frequency response of probe sensors and computerized processing have opened a whole new range of pressure, flow and geometrical measurements that have been previously impossible to perform.

Typically, the physician first selects the appropriate treatment method from among medication therapy, transcatheter cardiovascular therapeutics (TCT), coronary

artery bypass grafting (CABG), or non-treatment. Atherosclerotic lesions may have different characteristics. Some lesions exhibit a variable degree of calcification while others have a fatty or thrombotic nature. Lesion characteristics together with vessel condition proximal and distal to the lesion are the major factors for determining the therapeutic procedure needed. Recently, increasing numbers of patients have been directed toward TCT. TCT starts with an interventional diagnosis procedure (angiography), followed by the treatment of the patient with medication therapy, CABG or continuation of the TCT procedure with adequate interventional treatment.

Numerous methods are currently available for treating various lesion types. Some of these methods are given hereinbelow, sequenced from "softer" to "heavier", relating to their ability to open calcified lesions; percutaneous transluminal angioplasty (PTCA), "Cutting balloon" angioplasty, directional coronary atherectomy (DCA), rotational coronary atherectomy (RCA), Ultrasonic breaking catheter angioplasty, transluminal extraction catheter (TEC) atherectomy, Rotablator atherectomy, and excimer laser angioplasty (ELCA). Often, stents are placed within the lesion so as to prevent re-closure of the vessel (also known as recoil). If the stent is malpositioned, it interrupts the flow and may initiate restenosis.

Lesion characteristics, together with vessel condition proximal and distal to the lesion, are used to determine the medically and economically optimal treatment method or combination of methods of choice. Angiography has been the main diagnostic tool in the cath lab. The physician uses the angiographical images in order to identify and locate the lesions, evaluate the occlusion level (percentage of normal diameter) and qualitatively estimate the perfusion according to "thrombolysis in myocardial infarction" (TIMI) grades, determined according to the contrast material appearance. TIMI grades 0,1,2,3 represent no perfusion, minimal perfusion, partial perfusion and complete perfusion, respectively.

Among the more sophisticated diagnostic tools are qualitative coronary angiography (QCA), intravascular ultrasound (IVUS) intravascular Doppler velocity sensor (IDVS) and intravascular pressure sensor (IPS). QCA calculates geometrical properties from angiographic images, in image zones that are chosen by the physician.

IVUS provides accurate geometrical data regarding cross section area and accurate information regarding the vessel wall structure and composition. IDVS provides

velocity measurements, enabling discriminating various degrees of occlusion according to coronary flow reserve (CFR) criteria. IDVS suffers from inaccuracy problems resulting from positioning errors within the vessel. IPS provides pressure measurements enabling discriminating various degrees of occlusion according to the FFR (fractional flow reserve) criteria. Angiography and the sophisticated techniques discussed above may be employed prior to and after the therapeutic procedure (the last for the evaluation of the results and decision about correcting actions).

Unfortunately, the above discussed sophisticated methods are not commonly used due to their high price and operation complexity.

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#### OBJECTS AND SUMMARY OF THE INVENTION

This invention provides a medical intratherapeutic diagnostic system includes a signal analyzer and pressure sensor device adapted for use in the fluid delivery system of a living body such as a blood vessel system. The system measures flow disturbance found within the blood vessel for the purpose of determining the characteristics of the blood vessel walls including indications of stenosis, aneurisms, therapeutic success (balloon dilatation, dissection or stent malpositioning). The flow disturbance measured is created by the blood flow within areas of atherosclerotic occlusion of blood vessels. The system of the present invention increases the amount of knowledge available to the treating physician about the occlusion size and blood flow capacity. When natural blood flow is too low for flow disturbance induction, flow augmentation methods: vasodilatation (increases blood flow), injection of a controlled bolus of saline may be used to create measurable flow disturbance. Blood rheological characteristics, where known, may be included in computation procedure. The method is applicable also for by pass grafts evaluation and heart valves. Lastly, the present invention is applicable to other biological flow conduits (e.g. urine).

It is an object of the present invention to determine the flow disturbance characteristics in blood vessels.

It is a further object of the present invention to detect and characterize partial occlusions or aneurysms in blood vessels or in tubular flowing fluid conduits within a body.

It is an advantage of the present invention to measure the value of blood pressure or blood flow velocity as a function of time at multiple points within the blood vessel.

It is another advantage to evaluate the success of clinical treatment such as tracking sufficient opening of the occlusion or malpositioning of a stent.

5 It is yet another advantage that while the present invention is adopted to measurements and determination in blood vessels, the present invention can also be adopted for use in any tubular conduit containing fluid flow, such as urine flow in the urethra.

10 Additionally, an advantage of the present invention is its adaptability for use in other non-biological conduits having pulsatile flow within, such as water pipes through which pulsatile flow may be induced for measuring and characterizing internal narrowing due to scale deposits.

15 It is a feature of the present invention to calculate and report the determined flow disturbance parameters such as the maximal turbulence intensity and the spectral bandwidth that can be calculated and reported in absolute terms or as a ratio of the relevant parameter value in the lesioned region to the parameter value in a non-lesioned region of the same patient.

20 It is a further feature to calculate and report a ratio of the relevant parameter determined in normal unstressed condition compared with a highly stressed condition where such a highly stressed condition maybe vasodilatation induced by injection of vasodilator such as papaverine.

It is yet another feature to characterize flow disturbances that are involved in biological processes within the vessel wall for predicting lesion development including stenosis initialization, plaque growth, plaque rupture and angiogenesis.

25 The objects, advantages and features of the present invention are embodied in a system for measuring turbulence of fluids communicated within a fluid delivery system of living body that includes at least one pressure sensor device adapted for insertion into the fluid delivery system and a signal analyzer connected to said pressure sensor device and operative to pressure signals generated by said pressure sensor device. The signal analyzer 30 is operative to measure and record a value of turbulence intensity.

In one embodiment, the system sensor device includes a plurality of pressure sensors wherein at least one of said plurality of pressure sensors is a wire. In another embodiment the pressure sensor is a fluid filled pressure transducer. The pressure sensor device includes a lumen catheter for locating said fluid filled pressure transducer in signal communication with said fluid delivery system.

5 In another embodiment, at least one of said plurality of pressure sensors is connected to a guidewire.

The system signal analyzer includes a computer adapted by a first software program to measure and record pressure signals of the fluid delivery system. The data is 10 subsequently recorded for later processing off-line.

The system signal analyzer also includes a second software program whereby said computer is adapted to determine a value for turbulence intensity within said fluid delivery system. The values of turbulence intensity and related measurements maybe used to determine stenosis characteristics with the fluid delivery system.

15 The system includes a method for measuring flow disturbances of fluids within a fluid delivery system of a living body comprising the steps of:

providing a data acquisition system having at least one pressure sensor device and a signal analyzer operatively connected to the pressure sensor device to receive 20 pressure signals;

inserting and locating the pressure sensor device within the fluid delivery system at a first location;

measuring the pressure at the first location;

moving said pressure sensor device by a predetermined distance to a second 25 location;

measuring the pressure at the second location;

repeating said moving and measuring steps to obtain a plurality of locations;

calculating a spectrum bandwidth and turbulence intensity for each of said 30 locations.

The method steps of moving, measuring and calculating are repeated until the data has accurately measured the features of turbulence intensity.

In addition, this invention provides a system wherein said computer is adapted by said second program to determine an aneurism based upon said length of said turbulence zone. Such a system serves as an evaluation tool for identifying malpositioned stents which create flow disturbances, traced by pressure (similar to stenosis). Further, the 5 system is used for localization of drug delivery when said computer is adapted by said second program to determine a shear stress within said blood vessel system.

Further, if blood rheology is known (mainly viscosity), flow disturbance parameters may be modified to consider those, which may be done either manually or automatically.

10 Lastly, flow disturbance identification and quantification may be useful in treatment and diagnosis of heart valves, both diagnosis of natural ones and evaluation of performance of implanted ones: either artificial graft valves or tissue valves. Flow disturbance identification and quantification may be useful in treatment and diagnosis of by pass grafts, especially evaluating the stitches.

15

### BRIEF DESCRIPTION OF THE DRAWINGS

The present invention will be understood and appreciated more fully from the following detailed description taken in conjunction with the appended drawings in which like components are designated by like reference numerals:

5       Figure. 1 is a schematic isometric view of a system for lesion identification and determination of lesion severity, maximal flow, maximal velocity, shear stress and shear stress time derivative, constructed and operative in accordance with a preferred embodiment of the present invention;

10      Figure. 2 is a schematic isometric view of a system for lesion identification and determination of lesion severity, maximal flow, maximal velocity, shear stress and shear stress time derivative, constructed and operative in accordance with another preferred embodiment of the present invention;

15      Figure. 3 is a schematic functional block diagram illustrating the details of the system 1 of Figure. 1;

20      Figure. 4 is a schematic functional block diagram illustrating the details of the system 1.a of Figure. 2

Figure. 5 is a schematic isometric view of an in-vitro system, constructed and operative in accordance with a preferred embodiment of the present invention;

25      Figure. 6 is a schematic detailed illustration of the in-vitro tubing system 51 of Figure.5.

Figure. 7 is a schematic description of the in vitro system together with its control and monitoring equipment.

Figure. 8 is a detailed schematic illustration of the clinical system using single pressure sensor, describing the initial location of the sensor inside a blood vessel.

25      Figure. 9 is a detailed schematic illustration of the clinical system described in Figure 8, during operation.

Figure. 10 is a schematic graph illustrating the variation of the calculated spectral bandwidth values as a function of the distance from the stiff tube section of Figure. 9.

30      Figure. 11 is a detailed schematic illustration of the clinical system using two pressure sensors.

Figure.11A describes another version of the clinical system of Figure 11 using a fluid filled pressure sensor replacing the proximal pressure sensor of Figure 11.

Figure.12 is a graph representing the pressure raw data of a typical measurement as measured in the in vitro system using two pressure sensors..

5 Figure. 13 is a graph representing the turbulence intensity calculated from the raw pressure data of curve 75 of Figure. 12.

Figure. 14 is a graph representing the turbulence intensity calculated from the raw pressure data of curve 76 of Figure. 12

10 Figure.15 is a graph representing the pressure power spectrum calculated from the raw pressure data of curve 75 of Figure. 12.

Figure.16. is a graph representing the pressure power spectrum calculated from the raw pressure data of curve 76 of Figure. 12.

Figure 17 is a graph representing the pressure raw data of a typical measurement as measured in the in vitro system using two pressure sensors and glycerin solution.

15 Figure18 is a graph representing the pressure power spectrum calculated from the raw pressure data of curve 85 and of Figure. 17.

Figure19 is a graph representing the pressure power spectrum calculated from the raw pressure data of curve 86 and of Figure. 17.

### DETAILED DESCRIPTION OF THE PRESENT INVENTION

The present invention provides a method and system for determining flow disturbances in a vessel. Such determinations provide the detection and characterization of the vessel in regard to stenosis. The determination of flow disturbances is based on vortex generation in the vessel, by specifically, measuring and determining the spectrum bandwidth of the pressure signal in multiple areas of the vessel. As determined herein, a wider bandwidth means that there is a large stenosis, whereas where the bandwidth is smaller there is a smaller stenosis.

This invention provides a medical diagnostic methods and system which includes a signal analyzer and pressure sensor device adapted for use in the fluid delivery system of a living body such as a blood vessel system. The system measures turbulence found within the blood vessel for the purpose of determining the characteristics of the blood vessel walls including indications of stenosis. The turbulence measured is created by the reduced blood flow found within areas of atherosclerotic occlusion of blood vessels. The system of the present invention increases the amount of knowledge available to the treating physician about the occlusion size and blood flow capacity.

Reference is now made to Figures. 1, 2, 3 and 4. Figures. 1 and 2 present a schematic isometric view of a system for lesion identification and determination of lesion severity, maximal flow, maximal velocity, shear stress and shear stress time derivative

The system is constructed and operative in accordance with two embodiments of the present invention (1 and 2). Figure. 3 and 4 are schematic functional block diagrams illustrating the details of the system 1 of Figure. 1 and system 2 of Figure. 2.

The systems 1 and 2 include pressure sensor catheter or guide wire 4, inserted into the vessel directly or via a catheter lumen 3 for measuring the pressure inside a blood vessel. The lumen catheter type can include: a guiding catheter such as the type 8F Archer coronary guiding catheter sold by Medtronic Interventional Vascular, Minneapolis, U.S.A.; a diagnostic catheter such as the type SiteSeer diagnostic catheter sold by Bard Cardiology, U.S.A.; a balloon catheter such as the type Supreme fast exchange PTCA catheter sold by Biotronik GMBH & Co, U.S.A.; or any other conventional hollowed catheter. System 1 and system 2 include at least one sensor 4.

It will be appreciated that a number of pressure sensor configurations may be contemplated without departing from the scope of the present invention. For example, in one embodiment system 1 and 2 includes two (4a, 4b) pressure sensor catheters (not shown) or guide wires for measuring the pressure inside a blood vessel. Alternatively, 5 when using two pressure sensors a fluid filled (FF) pressure transducer 31, as described in Figures 1 and 2 is acceptable as well and is included in the system replacing one of the two pressure sensors 4A or 4B. In such a case the FF pressure transducer is connected via the end of the guiding catheter 3. In an exemplary embodiment, the pressure sensor 4 is of the type sold as the 3F one pressure sensor model SPC-330A or dual pressure catheter 10 SPC-721, commercially available from Millar Instruments Inc., TX, U.S.A. Other commercial pressure catheters suitable for diagnostic or combined diagnostic/ treatment purposes are also suitable for the present invention such as a 0.014 " guidewire mounted pressure sensor type sold as product number 12000 from Radi Medical Systems, Upsala, Sweden, or a Cardiometrics WaveWire pressure guidewire from Cardiometrics Inc., an Endsonics company of CA, U.S.A.

The system 1 and 2 also include a signal conditioner 23. A signal conditioner of the type suitable for this purpose is model TCB-500 control unit commercially available from Millar Instruments, or Radi Pressure Wire Interface Type PWI10, Radi Medical Systems, Upsala. The signal conditioner 23 is operatively connected to the pressure sensor 4 for amplifying the signals of the pressure sensor. The system 1 further includes an analog to digital (A/D) converter 28 connected to the signal conditioner 23 and to the FF pressure transducer 31 for receiving the analog signals therefrom. An A/D converter of the type suitable for this purpose is NI E Series Multifunction I/O model PCI-MIO-16XE-10 commercially available by National Instruments, Austin, TX. The signal conditioner 23 depends on the specific type of pressure sensors used and is preferably integrated in the 20 data acquisition card of the computer 20 or omitted altogether.

The system 2 of Figure. 2 also includes a standard cardiac catheterization system 22 that functions as a monitoring system. A standard cardiac catheterization system of the type suitable for this purpose is Nihon Kohden Model RMC-1100, commercially available 25 from Nihon Kohden Corporation, Tokyo, Japan. The signal conditioner 23 and the FF pressure transducer 31 are directly connected to the monitoring system 22. System 2

further includes an analog to digital (A/D) converter 28 connected to the output of the monitoring system 22 through a shielded I/O connector box 27. A connector box of the type suitable for this purpose is NI SCB-68 or BNC-2090 commercially available from National Instruments, Austin, TX.

5       The systems 1 and 2 also include a signal analyzer 20 connected to the A/D converter 28 for receiving the digitized conditioned pressure signals from the A/D converter 28. The signal analyzer 20 includes a computer 25 having a user interface that preferably includes a display 21 connected to the computer 25 for displaying text numbers and graphs representing the results of the calculations performed by the computer 25. The  
10      computer is connected to an archival device such as a network storage device or a printer represented by reference numeral 26 and operatively connected to the computer 25 for providing a hard copy of the results for documentation and archiving. It will be appreciated that the A/D converter 28 can be a separate unit or can be integrated in a data acquisition computer card installed in the computer 25 (not shown). The computer 25 processes the  
15      pressure data, sensed by the pressure sensors 4 and acquired by the A/D converter 28 or the data acquisition card (not shown) and generates textual, numerical and/or graphic data that is displayed on the display 21.

The computer 25 of systems 1 and 2 is adapted by the use of a data recording program to measure and record the pressure data within the blood vessel. Following the  
20      measurement procedure computation of the recorded data is required by a second program operating within the computer 25 to determine check for the predetermined blood vessel characteristics. In another embodiment the computer 25 of systems 1 and 2 is adapted by the use of an on-line data recording program to measure and record the pressure data within the blood vessel in real time. Following the measurement procedure

25       In order to fully appreciate the nature and character of the software program, it is necessary to first review the underlying principles of fluid dynamics in the blood vessel.

Generally, fluid flow in a straight tube is characterized by a Reynolds number  
R = u d / v. Wherein u is the mean fluid velocity, d is the tube diameter and v is  
30      the fluid viscosity. For steady state flow in a cylindrical tube the critical Reynolds number, R<sub>cr</sub>, is in the range of 1500-3000. For pulsatile flow the critical Reynolds number relates

directly to the frequency parameter  $\alpha$ . Thus,  $R_{cr} = K \cdot \alpha$ , wherein  $K$  is a constant in the range of 250-400,  $\alpha^2 = d^2(\omega/v)$  and  $\omega$  is the frequency of the pulsatile flow.

The pulsatile flow becomes turbulent if the maximal Reynolds number  $R_{max} = u_{max}d/v$  is larger than the critical Reynolds number  $R_{cr}$ , wherein  $u_{max}$  is the 5 maximal flow velocity during one cycle of the pulsatile flow. Thus

$$\frac{u_{max}d}{v} > K \cdot d \cdot \sqrt{\frac{\omega}{v}}$$

Thus, in a blood vessel, the transition from laminar to turbulent flow is determined by the value of  $u_{max}$ , the flow frequency  $\omega$  and the blood viscosity  $v$ . If

$$\frac{u_{max}}{\sqrt{\omega v}} > K, \text{ the flow becomes turbulent. In humans, } \omega \text{ is the heart beat frequency.}$$

10 For a heart rate of 60 beats/min,  $\omega \approx 2\pi(1/\text{sec})$ . The human blood viscosity is  $v \approx 4 \cdot 10^{-6}$  ( $\text{m}^2/\text{sec}^2$ ). Hence, the blood flow becomes turbulent if  $u_{max}$  is greater than approximately 1.5 m/sec. In cases of flow separation the transition to turbulence at the region downstream of a stenosis may occur at lower Reynold numbers.

15 The maximum velcoity in the human artery isapproximately 1m/s. If maximal velocity in the stenosis region is proportional to the blood vessel's cross sectional area reduction, we may expect turbulence for percent stenosis levels of 30 -50%. The percent stenosis is usually defined as the ratio of the stenosed vessel cross sectional area to the vessel's nominal (non-stenosed) cross sectional area. Stenosis in the range of 30-50% does not normally cause a significant flow reduction. Percent stenosis values of less than 20 approximately 50% result in transition to turbulence only in the flow separation region downstream of the stenosis. The separation region is defined as the region between the flow separation and flow reattachment points.

25 Downstream of the flow separation point, pressure turbulence intensity increases. Beyond the reattachment point, turbulence production ceases and turbulence intensity decays. Analysis of the change of turbulence intensity along the vessel longitudinal axis allows estimating the axial positions of the separation and the reattachment points. The percent stenosis may then be estimated from the length of the separation region.

Using pressure signals, the pressure turbulence intensity  $P_t$  may be calculated

using the equation:  $P_t = \frac{(P - \bar{P})^2}{\bar{P}}$  wherein  $P$  is the measured pressure signal and  $\bar{P}$

is the mean pressure calculated from the entire measurement period.

For turbulent flow,  $\omega_{max}/\omega = (R/R_{cr})^{3/4}$ , wherein  $\omega_{max}$  is the frequency of the  
5 smallest vortices and  $\omega$  is the heart beat frequency. Thus,  $\omega_{max}/\omega$  is proportional to

$(u_{max}/\sqrt{\omega v})^{3/4}$ . The measured value of  $\omega_{max}$  for turbulent flow is related to the value of

$u_{max}$  within the stenosis. If the minimal diameter of the stenosis  $d_{min}$  is independently determined, for example from independently performed QCA data, the maximal shear stress  $\tau_{max}$  may be estimated by using an equation for turbulent flow in a straight tube:

$$10 \quad \tau_{max} = 0.0655 \rho \frac{u_{max}^2}{2} \left( \frac{u_{max} d_{min}}{2v} \right)^{-1/4}$$

In pulsatile flow, the time of transition from laminar to turbulent flow is  $t_c$  which can be experimentally determined. Using an empirically determined value of the critical Reynolds number  $R_{cr}$  and the independently obtained value of  $d_{min}$ , the critical velocity  $u_{cr}$  is defined as  $u_{cr} = R_{cr} \cdot v / d_{min}$ . The laminar shear stress  $\tau_{cr}$  at time point  $t_{cr}$  may be

15 calculated using the shear stress equation for the laminar case  $\tau_{cr} = \frac{32 \rho v u_{cr}}{d_{min}}$ , wherein  $\rho$  is blood density. Assuming maximal velocity is achieved at the time of maximal turbulent intensity, the derivative  $dt/dt$  may be estimated as  $(\tau_{max} - \tau_{cr})/\Delta t$ , wherein:  $\tau_{max}$  is the maximal shear stress,  $\tau_{cr}$  is the laminar shear stress,  $\Delta t$  is the time interval between  $t_{cr}$  and 20 the empirically determined time point at which turbulence intensity reaches its maximum.

## IN VITRO EXAMPLES APPARATUS

Reference is now made to Figures. 5, 6 and 7. Figure. 5 is a schematic diagram representing an in-vitro experimental apparatus constructed and operative for determining flow characteristics in simulated non lesioned and lesioned blood vessels, in accordance 25 with an embodiment of the present invention. Figure. 3 is a schematic functional block

diagram illustrating the functional details of a system including the apparatus of Figure. 5 and apparatus for data acquisition, analysis and display.

The fluidics system 51 of Figure. 5 is a recirculating system for providing pulsatile flow. The system 51 includes a pulsatile pump 42 model 1421A pulsatile blood pump, commercially available from Harvard Apparatus, Inc., Ma, U.S.A., however other suitable pulsatile pumps can be used. The pump 42 allows control over rate, stroke volume and systole/diastole ratio. The pump 42 re-circulates distilled water from a water reservoir 15 to a water reservoir 14.

The system 51 further includes a flexible tube 43 immersed in a water bath 44, 10 to compensate for gravitational effects. The flexible tube 43 is made from Latex and has a length of 120 cm. The flexible tube 43 simulates an artery. The flexible tube 43 is connected to the pulsatile pump 42 and to other system components by Teflon tubes. All the tubes in system 51 have 4 mm internal diameter. A bypass tube 45 allows flow control in the system and simulates flow partition between blood vessels. A Windkessel 15 compliance chamber 46 is located proximal to the flexible tube 43 to control the pressure signal characteristics. A Windkessel compliance chamber 47 and a flow control valve 48 are located distal to flexible tube 43 to simulate the impedance of the vascular bed.

The system 51 of Figure. 5 also includes a flowmeter 11 connected distal to the flexible tube 43 and a flowmeter 12 connected to the bypass tube 45. The flowmeters 11 and 12 are 20 suitably connected to the A/D converter 28. The flowmeters 11 and 12 are model 111 turbine flow meters, commercially available from McMillan Company, TX, U.S.A.. In certain cases, an ultrasonic flowmeter model T206, commercially available from Transonic Systems Inc., NY, U.S.A is used.

Reference is now made to Figure. 6, which is a schematic cross sectional view 25 illustrating a part of the fluidics system 51 in detail. An artificial stenosis made of a tube section 55, inserted within the flexible tube 43 is described. The tube section 55 is made from a piece of Teflon tubing. The internal diameter 52 (not shown) of the artificial stenosis 55 may be varied by using artificial stenosis sections fabricated separately and having various internal diameter.

30 Pressure is measured along the flexible tube 43 using a pressure measurement system including MIKRO-TIP pressure catheters 57,58 and 59, model SPR-524 pressure

catheter, connected to a model TCB-500 control unit, commercially available from Millar Instruments Inc., TX, U.S.A.. The catheters 57,58 and 59 are inserted into the flexible tube 43 via the connector 10, connected at the end of the flexible tube 43. The catheters 57,58 and 59 include pressure sensors 24A, 24B and 24C, respectively, for pressure measurements. A fluid filled pressure transducer 31 is connected to the system 51 via the end of the guiding catheter 3, inserted into the flexible tube 43 via the connector 9. The fluid filled pressure transducer 31 is connected to the system 51, when additional pressure readings are needed, or in place of an intravascular pressure transducer, according to the defined experiment.

Reference is now made to Figure. 7. The system 41 includes the system 51. The system 41 also includes a signal conditioner 23 model TCB-500 control unit commercially available from Millar Instruments. The signal conditioner 23 is suitably connected to the pressure sensors 24A, 24B and/or 24C for amplifying the pressure signals

Data acquisition was performed using a PC (Pentium 586) with an E series Instruments multifunction I/O board 28 model PC-MIO-16E-4, commercially available from National Inc., TX, U.S.A. The I/O board was controlled by a Labview graphical programming software, commercially available from National Instruments Inc., TX, U.S.A. 10 sec interval of pressure and flow data were sampled at 5000Hz, displayed during the experiments on the monitor and stored on hard disk. Analysis was performed offline using Matlab version 5 software, commercially available from The MathWorks, Inc., MA, U.S.A.

## IMPLEMENTATION METHODS

The method is based on performing pressure measurements at a plurality of points along a blood vessel in the region of a stenosis. Knowing the pressure versus time at these points enable the calculation of flow parameters indicating existence of flow disturbance caused by a stenosis, and deriving parameters which characterize the stenosis.

The general method is presented in the flow chart of Figure 30. The method can be implemented by using two clinical approaches. One is using a single pressure sensor and the second using two pressure sensors.

In both cases the following output can be obtained:

### 1. Lesion identification and location

The location of the stenosis may be determined by inspection (visually or computerized) of the variation of the spectrum bandwidth and the turbulence intensity in the region around stenosis. Such a variation is an indication of the existence of flow disturbance caused by a stenosis.

## 5 2. Stenosis severity

The separation region is defined as the region between the flow separation and flow reattachment point. Analysis of the change of turbulence intensity along the vessel longitudinal axis allows estimating the axial positions of the separation and the reattachment points of the flow. The percent stenosis may then be estimated from the length of the separation region.

10 The percent stenosis may also be determined by the maximal values of the spectrum bandwidth and the turbulence intensity as measured in the region around stenosis.

## 3. Maximal velocity ( $u_{\max}$ )

Maximal velocity is determined using the following equation:

$$15 \quad \omega_{\max} / \omega = K \left( \frac{u_{\max}}{\sqrt{\omega v}} \right)^{3/4}$$

$\omega$  : frequency of heart beats

$\omega_{\max}$  : frequency of smallest vortices

$v$ : blood viscosity

K : a constant that may be experimentally determined

## 20 4. Maximal Shear stress ( $\tau_{\max}$ )

Maximal shear stress is determined using the following equation:

$$\tau_{\max} = 0.0655 \rho \frac{u_{\max}^2}{2} \left( \frac{u_{\max} d_{\min}}{2v} \right)^{-1/4}$$

$\tau_{cr}$  is the laminar shear stress)

25 The laminar shear stress  $\tau_{cr}$  at time point  $t_{cr}$  may be calculated using the shear stress equation for the laminar case:

$$\tau_{cr} = \frac{32 \rho v u_{cr}}{d_{\min}}$$

the critical velocity  $u_{cr}$  is defined as:

$$u_{cr} = R_{cr} \cdot v / d_{min}$$

For pulsatile flow:

$$R_{cr} = K_1 \cdot \alpha$$

$K_1$  is a constant in the range of 250-400.

$$5 \quad \alpha^2 = d^2(\omega/v)$$

### 5. Shear stress derivative ( $d\tau/dt$ )

Assuming maximal velocity is achieved at the time of maximal turbulent intensity, the derivative  $d\tau/dt$  may be estimated:

$$10 \quad dt/dt = (\tau_{max} - \tau_{cr})/\Delta t$$

$\tau_{cr}$  is the laminar shear stress.

$\Delta t$  is the time interval between  $t_{cr}$  (time when  $\tau_{cr}$  occurs) and the empirically determined time point at which turbulence intensity reaches its maximum  $\tau_{max}$ .

## METHOD 1-SINGLE PRESSURE SENSOR

### CLINICAL SYSTEM

15 Reference is now made to Figure. 8 describing a cross section of an artery 30 having an arterial wall 32 and stenosis obstruction 34. A guiding catheter 3 (or diagnostic catheter, or any other hollowed catheter) is inserted into the blood vessel of interest. A single guide wire 7, having pressure sensor at its end, 4, is inserted trough the catheter and positioned so that the pressure sensor 4, is located at point A, proximal to the stenosis. The 20 catheter, guide wire and pressure sensor, are part of the clinical system described in Figures. 1 and 2.

### Data Acquisition

Data acquisition is performed using the clinical system described in Figure.

25 8.The steps used for data acquisition are :

1. Insert pressure sensor 4 into the artery.
2. Locate pressure sensor 4 at the zone of interest (point A proximal to the stenosis).
3. Measure the pressure at point A. then move the pressure sensor by a constant distance  $\Delta$  and measure the pressure.

4. Calculate the spectrum bandwidth and the turbulence intensity for each point (of step 3).
5. Calculate the average spectral bandwidth and averaged turbulence intensity from the data calculated in step 4. If variance is high, collect two more points and calculate new average. This data is used as "baseline data".
6. Move the pressure sensor 4 forward, again, by a distance  $\Delta$  (represented in Figure 9 by the double headed arrow labeled  $\Delta$ ) to a new point and perform pressure measurements as disclosed in step 3. (The in vitro experiments show that for this method the needed  $\Delta$  is about 1.5±2 cm, but this numbers could be slightly different for the cases of real artery stenosis).
7. Calculate spectrum bandwidth and turbulence intensity for the new point,
8. Compare the values of the turbulence intensity and the spectral bandwidth calculated for the new point to the baseline values.

If the calculated values of both these parameters for the new point are similar to both of the corresponding baseline parameters values, the pressure sensor 4 is advanced again by a distance .

If the calculated values of both, the turbulence intensity and the spectral bandwidth parameters, of the new point are larger then the baseline values, the pressure sensor 4 is retracted back by a distance  $\Delta$  to the previous point.

The process of measurement and calculation is now repeated for a new series of points, using a distance  $\Delta$ , until the calculated values of the turbulence intensity and the spectral bandwidth return to their values measured at the plurality of points which were initially measured proximal to the stenosis (step 3).

#### Data Analysis And Results

Analysis of the pressure data is performed to obtain turbulence intensity, maximal flow, pressure power spectrum and  $\omega_{max}$ . These calculated data are used to obtain values of stenosis location and severity, maximal velocity, maximal shear stress and shear stress time derivative using the equation and methods mentioned here in above.

**EXAMPLE 1**

Reference is now made to Figure. 9 which is a schematic representation of part of the in vitro system described in Figures. 5 and 6, modified for performing pressure measurements with a single pressure sensor 24a. The pressure catheter 3, guide wires 5 57,58 and its pressure sensors 24b and 24c were withdrawn from the system. Dynamic measurements of pressure pulsation were made by moving the pressure sensor 24a along points 60-71 of Figure. 9, which are positioned along the common longitudinal axis 72 of the flexible tube 43 and the stiff tube section 55.

Using these measurements the spectrum bandwidth and the maximal turbulence 10 intensity are calculated yielding identification of stenosis location and characteristics of the stenosis such as maximal flow.

The calculated values of the turbulence intensity and the spectral bandwidth of all the points are now plotted as a function of the distance step or an arbitrary distance along the longitudinal axis of the flexible tube 3 representing the stenosis.

15 The location and the percent stenosis may be determined visually by the operator of the system or computed automatically by a computer analysis of the variation of the spectrum bandwidth and the turbulence intensity in the region around stenosis.

Reference is now made to Figure. 10 describing a schematic graph (curve 74) illustrating the variation of the calculated spectral bandwidth values as a function of the 20 distance from the stiff tube section 55 of Figure. 9. The location of the stiff tube is indicated by arrow 73. The vertical axis represents the spectral bandwidth and the horizontal axis represents the distance along the longitudinal axis 72 (Figure. 9) in centimeters. It is noted that distance value 0, is arbitrarily chosen to correspond with the longitudinal position of the proximal end 55A of the 2 cm long stiff tube section 55. 25 Positive distance values represent points distal to the end 55A and negative distance values represent points proximal to the end 55A.

TABLE 1 summarizes Calculated results of turbulence intensity and spectral bandwidth as calculated from pressure measurements in an experiment where the area reduction was 44%.

TABLE 1

Distance from the stenosis	Spectrum bandwidth	Max. Turbulence Intensity %
-3	50	0.4
-2.5	50	0.4
-2	50	0.4
-1.5	50	0.4
-1	50	0.4
-0.5	50	0.4
0	50	0.4
0.5	50	0.4
1	50	0.4
1.5	50	0.42
2	50	0.4
2.5	65	0.5
3	240	0.44
4	220	0.4
4.5	160	0.37
5	60	0.38

It is noted that, no indication of turbulence is seen proximal to and within the  
 5 stiff tube section 55 representing the stenosis.

The curve 74 of Figure. 10 represents a curve that was fitted to the points of the calculated values of the spectral bandwidth given in TABLE 1. The increase in the calculated values of the spectral bandwidth starting at a distance value of approximately 2 cm indicates the presence of turbulent flow. The values of the spectrum bandwidth proximal to and within the stiff tube section 55 representing the stenosis are about 50 Hz, and do not change significantly until the pressure sensor 24A is about 2 cm distal to the proximal end 55A of the stiff tube section 55 representing the stenosis. This kind of flow behavior could be used during the diagnostic process in the cath lab.

It is noted that, in a clinical system, the variation of the values of the spectral bandwidth may enable the physician or the operator of the system to detect, localize and characterize also small stenosis that cannot be detected by angiography due to their small dimensions or to the limited spatial resolution of standard angiographic methods.

Thus, as illustrated in Figure.10 and demonstrated in TABLE 1, the spectrum bandwidth values indicate the presence of flow disturbances distal to a stenosis, and may therefore be used to identify the stenotic region. The above disclosed example and Figure.

10 indicate that the spectral bandwidth due to turbulence which occurs distal to the stenosis may provide an excellent indication of the position and character of a stenotic lesion in an artery.

It is noted that in the in-vitro system, the precise location of the sensor 24A can  
5 be directly measured. When the preferred embodiment of the present invention is adapted for performing similar measurements in vivo, the location of the tip of the pressure catheter may be determined by simultaneously obtaining angiographic data. This localization may be done for a single known point of measurements and the location of all the subsequent measuring points can then be calculated from the known distance increment  $\Delta$ .

10

## METHOD 2- DOUBLE PRESSURE SENSOR

### CLINICAL SYSTEM

Reference is now made to Figure. 11 describing a cross section of an artery 30 having an arterial wall 32 and stenosis obstruction 34. A guiding catheter 3 (or diagnostic catheter, or any other hollow catheter) is inserted into the blood vessel of interest. Two 15 guide wires, 6 and 7, having pressure sensors at their ends, 4A and 4B, are inserted trough the guiding catheter and positioned so that one pressure sensor 4A is located at point A proximal to the stenosis and the second pressure sensor 4B is located at point B, distal to the stenosis. Both pressure sensors are connected to a signal conditioner 23 as described in Figures. 1 and 2.

20

Reference is now made to Figure.11A describing another version of this clinical system. The pressure sensor 4A located at point A proximal to the stenosis is replaced by a fluid filled catheter connected at its external end to a pressure transducer measuring the pressure proximal to the stenosis. A single guide wire 6, having pressure sensor at its end, 4B, is inserted trough the fluid filled catheter and positioned so that the pressure sensor 4B is located at point B, distal to the stenosis.

25

### Data Acquisition

Pressure measurements are performed simultaneously by the two pressure sensors. The pressure sensor located proximal to the stenosis measure the pressure at the laminar flow zone at a fixed point proximal to the stenosis. The second pressure sensor

located distal to the stenosis is moved downstream and measure the pressure at plurality of points along the vessel, distal to the stenosis. The process of measurements and calculation, as described in example 1, is repeated again.

#### Data Analysis

5 Analysis of the pressure data is performed to obtain turbulence intensity, maximal flow, pressure power spectrum and  $\omega_{max}$ . These calculated data are used to obtain values of stenosis location and severity, maximal velocity, maximal shear stress and shear stress time derivative using the equation and methods mentioned here in above.

#### EXAMPLE 2

10 Measurements of pressure pulsation were made using the in vitro system described in Figures 5 and 6, locating two pressure sensors 24a and 24b upstream and downstream of the stiff tube section 55. The blood vessel was modeled by flow of distilled water in a flexible tube 43 with inner diameter of 4 mm. The pressure sensor 24A was positioned 1cm proximal to the stiff tube section. The pressure sensor 24B was located 15 distal to the stiff tube section. For each measurement, the flow was calculated from the pressure data of sensors 24A and 24B according to the following equation:

$$q = \frac{A_0}{\sqrt{\left(\frac{A_0}{A_s}\right)^2 - 1}} \sqrt{\frac{2 \Delta P}{\rho K_t}}$$

wherein:

A<sub>0</sub> is the nominal cross sectional area of flexible tube 43.

20 A<sub>s</sub> is the cross sectional area represented by the internal diameter of the stiff tube section 55.

ΔP is the pressure difference measured by the sensors 24A and 24B across the stiff tube representing the stenosis.

θ is the water density.

25 constant K<sub>t</sub>=1.52.

For every measurement, analysis of the turbulence intensity P<sub>t</sub> and the power spectrum of the pressure was performed. The pressure turbulence intensity P<sub>t</sub> is defined as

$P_t = \frac{(P - \bar{P})^2}{\bar{P}}$  wherein P is the measured pressure signal and  $\bar{P}$  is the mean pressure calculated from the entire measurement period (10 sec).

Reference is now made to Figure 12. Figure 12 is a graph representing the pressure raw data of a typical measurement. The measurement was performed using a stiff tube 55 having an internal area reduction of 94%. The vertical axis represents the pressure in mm Hg and the horizontal axis represents the time in sec. The curve 75 represent the pressure measured proximal to the stiff tube section (by sensor 24A). Curve 76 represents the pressure measured distal to the stiff tube section (by sensor 24B).

Reference is now made to Figures. 13 and 14, which are graphs representing the turbulence intensity calculated from the raw pressure data of curve 75 and curve 76 of Figure. 12, respectively. The vertical axis of Figures 13 and 14 represent the turbulence intensity  $P_t$  (in %), and the horizontal axis of represent time (in seconds). Curve 77 of Figure. 13 represents the turbulence intensity calculated from the raw data of curve 75 of Figure. 12. Curve 78 of Figure. 14 represents the turbulence intensity calculated from the raw data of curve 76 of Figure. 12.

Figures.15 and 16 represent the pressure power spectrum calculated from the raw pressure data of curve 75 and curve 76 of Figure. 12, respectively. Curve 79 of Figure. 15 represents the pressure power spectrum calculated from the raw data of curve 75 of Figure. 12 and curve 83 of Figure. 16 represents the pressure power spectrum calculated from the raw data of curve 76 of Figure. 12. It is noted that, the vertical axes of Figures. 15 and 16 is a logarithmic scale.

Plotting the power spectrum of Figure. 16 on a semi-logarithmic scale yields a signal approximated by two straight lines 80 and 81 intersecting at the point 82 representing the frequency  $\omega_{max}$ .

The straight lines 80 and 81 were hand fitted to the curve 83, but can be achieved by known statistical procedures such as least-mean-square or by any other suitable method. The flow and its maximum are calculated from the measured pressure data.

The results of the analysis for various flow levels performed for the same stenosis (94% area reduction); are summarized in table 2.

In another example, the method is executed using a single transducer moving from location A to B, gated to either ECG or Fluid Filled. The transducer measuring turbulence has a high bandwidth (500hz at least). For example, to calculate hemodynamic parameters, simultaneous pressure at points A and B during rest and vasodilatation are required. The pressures at points A and B during rest are measured, but non-simultaneously. Time synchronization is performed using the idea that the ECG signals are stable while measuring pressure at points A or B. Therefore, synchronizing the ECG signals, results in synchronization of the pressure signals at points A and B. Synchronization is achieved by applying Algorithm 2, with the ECG signals used instead of the fluid filled pressure signals. For the vasodilatation condition, it is possible to measure pressure only at point B (downstream). The enlargement of the vessel wall during vasodilatation is negligible proximal to the stenosis, at point A. The simultaneous pressures at point A and B during vasodilatation is calculated.

TABLE 2:

Stenosis	Lb * [cm]	Calculated turbulence intensity (%)	Calculate $d\omega_{max}$ (Hz)	Calculated Maximal Flow [cc/min]
94%	1	3-4%	1400	200
94%	1	2%	1000	160
94%	1	1.5%	750	125

15.

\* Where Lb is the distance between the pressure sensor 24B and the distal end of the stiff tube 55 representing the stenosis.

As can be seen from the results in TABLE 2, Turbulence intensity and  $\omega_{max}$  vary as a function of the flow. The data presented in TABLE 2 are calculated at maximal turbulent intensity. The suggested relationship between turbulence intensity,  $\omega_{max}$  and maximal flow is demonstrated here for severe (94%) stenosis. As flow depends on the stenosis size (type), knowing the turbulence intensity and  $\omega_{max}$  allow distinguishing between stenosis types.

**EXAMPLE 3**

Measurements of pressure pulsation were made using the in vitro system described in Figures 5 and 6, by using two pressure sensors 24a and 24b. Pressure sensor 24a was located upstream of the stiff tube section 55, 2 cm proximal to the stiff tube proximal section. Pressure sensor 24b was moved by steps from point located 0.5 cm proximal to the stiff tube section 55 distal end, to a point located 3 cm distal to the stiff tube section 55 distal end. The blood vessel was modeled by flow of distilled water in a flexible tube 43 with inner diameter of 4 mm. After each step pressure was measured by the two pressure sensors.

This procedure was repeated three times using three different stiff tubes (55), having different internal diameter representing various levels of stenosis.

For each measurement, the frequency  $\omega_{\max}$ , was calculated from the pressure data of sensors 24b.

The results of the analysis for this series of simulations pressure measurements, performed for different sizes stenosis (93.75%, 86%, 43.75% area reduction), are summarized in table 3.

**TABLE 3**

$L_b$ [cm]	93.75% stenosis		86% stenosis		43.75% stenosis	
	$\omega_{\max}$ (Hz)	Turbulence intensity	$\omega_{\max}$ (Hz)	Turbulence intensity	$\omega_{\max}$ (Hz)	Turbulence intensity
-0.5	----	-----	1700	0.07	100	0.1311
0.0	----	-----	1500	0.084	50	0.13
0.5	1600	0.0365	1000	0.0833	300	0.1336
1.0	1000	0.0344	380	0.0876	----	-----
1.5	500	0.0213	230	0.0854	200	0.1307
2.0	500	0.0186	250	0.081	140	0.1178
3.0	450	0.0351	200	0.0787	160	0.1132

Where  $L_b$  is the distance between the pressure sensor 24B and the distal end of the stiff tube 55 representing the stenosis.

As can be seen from the results in TABLE 3,  $\omega_{\max}$  and turbulence intensity varies as a function of the stenosis size. The suggested relationship between  $\omega_{\max}$ , turbulence intensity and area reduction of the vessel is demonstrated here for three levels of stenosis. Since  $\omega_{\max}$  and turbulence intensity depend on stenosis size, knowing these values allows distinguishing between stenosis types and to determine its severity rate.

It will be understood that certain features and sub-combinations are of utility and may be employed without reference to other features and sub-combinations as they are outlined within the claims. While the preferred embodiment and application of the invention has been described, it is apparent to those skilled in the art that the objects and features of the present invention are only limited as set forth in claims attached hereto.

#### EXAMPLE 4

Measurements of pressure pulsation were made using the in vitro system described in Figures 5 and 6, locating two pressure sensors 24a and 24b upstream and downstream of the stiff tube section 55. The blood vessel was modeled by flow of 40% Glycerin solution in a flexible tube 43 with inner diameter of 4 mm. The pressure sensor 24A was positioned 2 cm proximal to the stiff tube section. The pressure sensor 24B was located 1 or 2 cm distal to the stiff tube section. For each measurement, the flow was measured by the flow meter of the system and analysis of the power spectrum of the pressure was performed.

Reference is now made to Figure. 17, 18 and 19 which are examples of a single measurement results out of a series of measurements. Figure.17 is a graph representing the pressure raw data of a typical measurement. The measurement was performed using stiff tube 55 having an internal area reduction of 94%. The vertical axis represents the pressure in mm Hg and the horizontal axis represent the time in sec. The curve 85 represent the pressure measured proximal to the stiff tube section (by sensor 24A). Curve 86 represents the pressure measured distal to the stiff tube section (by sensor 24B).

Figures.18 and 19 are graphs representing the pressure power spectrum calculated from the raw pressure data of curve 85 and curve 86 of Figure. 17, respectively. Curve 87 of Figure. 18 represents the pressure power spectrum calculated from the raw data of

curve 85 of Figure. 17 and curve 88 of Figure. 19 represents the pressure power spectrum calculated from the raw data of curve 86 of Figure. 17. It is noted that, the vertical axis of Figures. 18 and 19 is a logarithmic scale.

Plotting the power spectrum of Figure. 19 on a semi-logarithmic scale yields a signal approximated by two straight lines 89 and 90 intersecting at the point 91 representing the frequency  $\omega\omega_{\max}$ .

The straight lines 89 and 90 were hand fitted to the curve 88 "by eye" but can be achieved by known statistical procedures such as least-mean-square or by any other suitable method.

The results of the analysis for various flow levels performed for the different stenosis (94% and 75% area reduction), are summarized in table 4.

TABLE 4:

Stenosis	$L_b$ [cm]	Flow [cc/min]	turbulence detection	Calculated $\omega_{\max}$ (Hz)
94%	1	33	Not detectable	---
94%	1	200	detectable	1120
94%	2	76	Not detectable	----
94%	2	125.9	detectable	250
75%	2	57.7	Not detectable	----
75%	2	199.3	detectable	226

\* where  $L_b$  is the distance between the pressure sensor 24B and the distal end of the stiff tube 55 representing the stenosis.

The purpose of these test examples is to demonstrate the existence and detection capability of the flow disturbance affect caused by stenosis in fluid having viscosity value almost similar to that of blood. As can be seen from the results in TABLE 4 flow disturbances were detected distal to stenosis for mild - severe stenosis type (94% and 75%). Low disturbance for lower flow level (around 100 ml/min) and more significant disturbances for higher flow level. For flow rate less than 100 ml/min no disturbance was

detected. The suggested relationship between  $\omega_{\max}$ , maximal flow and the level of stenosis shown in details in hear above, using distilled water, is shown to be relevant also in glycerin. The use of glycerin solution exhibit a damping effect which result in a delayed appearance of flow disturbances, only in more severe strnosis and higher flow levels,  
5 beyond normal physiological levels. this means that in a clinical system an artificial increases in flow should be induced. One common way already used in this arena is the use of vasodilatation which may well increase the flow to a level where flow disturbances are detectable.

**CLAIMS****What is claimed is:**

1. A system for measuring flow disturbances within a fluid delivery system of living body comprising:
  - 5 at least one pressure sensor device adapted for insertion into said fluid delivery system;
  - a signal analyzer connected to said pressure sensor device and operative to pressure signals generated by said pressure sensor device;
  - 10 said signal analyzer being operative to measure and record a value of turbulence intensity.
2. The system of claim 1 wherein said at least one sensor device includes a plurality of pressure sensors.
3. The system of claim 2 wherein at least one of said plurality of pressure sensors is a fluid filled pressure transducer and said at least one sensor device includes a lumen catheter for locating said fluid filled pressure transducer in signal communication 15 with said fluid delivery system.
4. The system of claims 2 or 3 wherein at least one of said plurality of pressure sensors is connected to a guidewire.
5. The system of claim 4 wherein said at least one pressure device includes a signal conditioner operatively connected to said pressure sensors.
- 20 6. The system of claim 1 wherein said signal analyzer includes a digital to analog converter connected to said at least one pressure sensor device.
7. The system of claim 5 wherein said signal analyzer includes an analog to digital converter connected to said signal conditioner.
- 25 8. The system of claim 1 wherein said signal analyzer includes a computer adapted by a first software program to measure and record pressure signals of said fluid delivery system.

9. The system of claim 1 wherein said signal analyzer includes a second software program whereby said computer is adapted to determine a value for turbulence intensity within said fluid delivery system.
10. The system of claim 9 wherein said computer is adapted by said second program to determine a stenosis value based upon said value of turbulence intensity.
11. The system of claim 9 wherein said computer is adapted by said second program to determine a flow frequency within an area of turbulent flow  $\omega_{\max}$ .
12. The system of claim 11 wherein said computer is adapted by said second program to determine a stenosis value based upon said flow disturbance frequency.
13. The system of claim 9 wherein said computer is adapted by said second program to determine a length of a turbulence zone.
14. The system of claim 13 wherein said computer is adapted by said second program to determine a stenosis value based upon said length of said turbulence zone.
15. The system of claim 9 wherein said fluid delivery system is a blood vessel system and said computer is adapted by said second program to determine a stenosis value based on flow frequency in a blood vessel of interest.
16. The system of claim 9 wherein said fluid delivery system is a blood vessel system and said computer is adapted by said second program to determine a stenosis value based upon a value of turbulence intensity along a blood vessel of interest.
17. The system of claim 9 wherein said fluid delivery system is a blood vessel system and said computer is adapted by said second program to determine a maximal velocity within said blood vessel system.
18. The system of claim 9 wherein said fluid delivery system is a blood vessel system and said computer is adapted by said second program to determine a shear stress within said blood vessel system.
19. The system of claim 9 wherein said fluid delivery system is a blood vessel system and said computer is adapted by said second program to determine a shear stress time derivative, indicating risk for plaque vulnerability within said blood vessel system.

20. A method for measuring turbulence of fluids within a fluid delivery system of a living body comprising the steps of:
  - providing a data acquisition system having at least one pressure sensor device and a signal analyzer operatively connected to said pressure sensor device to receive pressure signals;
  - inserting and locating said pressure sensor device within said fluid delivery system at a first location;
  - measuring the pressure at said first location;
  - moving said pressure sensor device by a predetermined distance to a second location;
  - measuring the pressure at said second location;
  - repeating said moving and measuring steps to obtain a plurality of locations;
  - calculating a spectrum bandwidth and turbulence intensity for each of said locations.
- 15 21. The method of claim 20 further comprising the step of calculating an average spectral bandwidth and average turbulence intensity.
22. The method of claim 21 further comprising the steps of determining whether additional location measurements are required and measuring pressure at least one additional location.
- 20 23. The method of claim 22 wherein said determining step includes checking for a high data variance.
24. The method of claim 22 further comprising the step of calculating a spectrum bandwidth and turbulence intensity for said additional locations.
- 25 25. The method of claim 24 further comprising the step of comparing spectrum bandwidth and turbulence intensity values of said additional locations with said averaged values.
26. The method of claim 25 further comprising the step of determining whether more locations are to be measured and repeating said measuring, calculating and comparing steps for said more locations.

27. The method of claim 26 further comprising determining whether said measurements are to be repeated.
28. The method of claim 27 repeating said moving and measuring steps.
29. The method of claim 1 comprising the step of determining stenosis severity using  
5 said value of turbulence intensity.
30. The method of claim 1 comprising the step of determining stenosis severity using the value of  $\omega_{\max}$ .
31. The method of claim 1 comprising the step of determining stenosis severity by the length of the turbulence zone
- 10 32. The method of claim 1 wherein said pressure measurements are within a blood vessel, said method comprising the step of determining stenosis location using the value of turbulence intensity along a blood vessel of interest.
33. The method of claim 1 wherein said pressure measurements are within a blood vessel, said method comprising the step of determining stenosis location using the  
15 value of  $\omega_{\max}$  along a blood vessel of interest.
34. The method of claim comprising the step of determining maximal velocity.
35. The method of claim 1 comprising the step of determining shear stress.
36. The method of claim 1 comprising the step of determining shear stress time derivative.

1/17

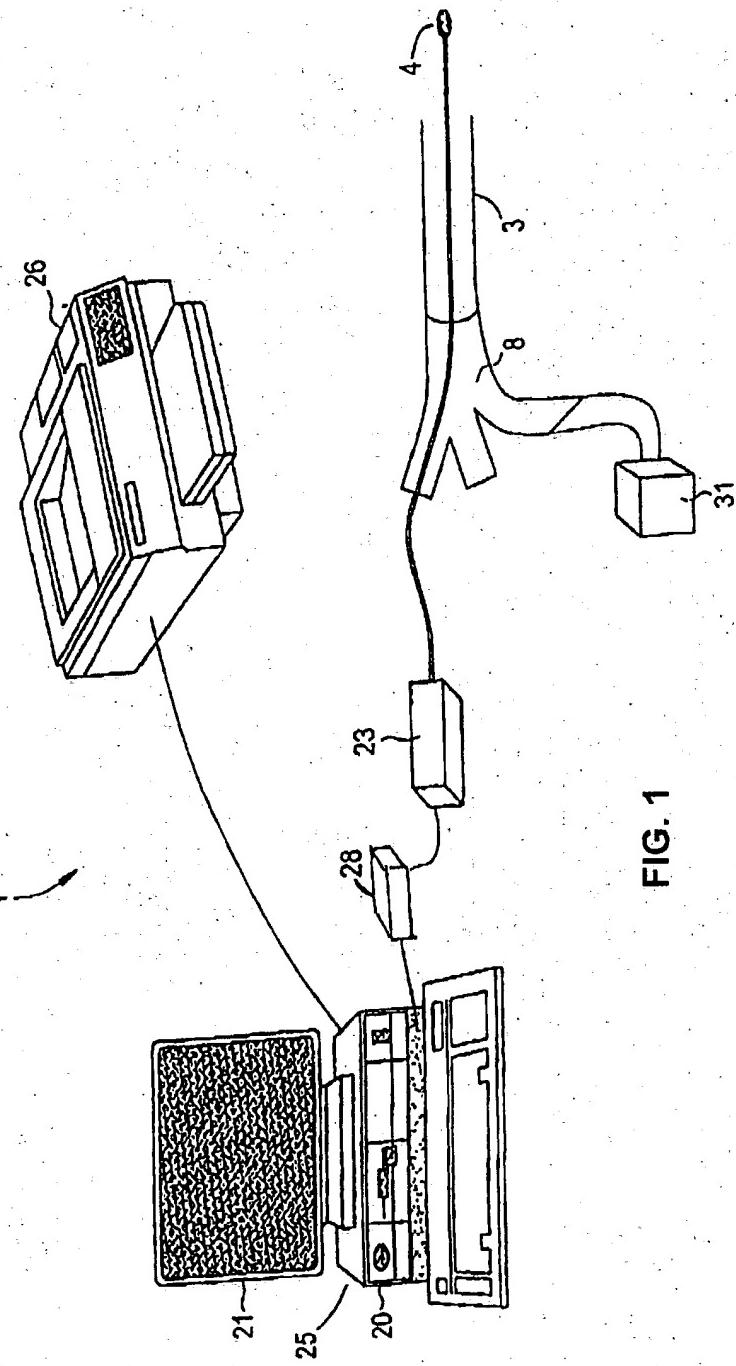
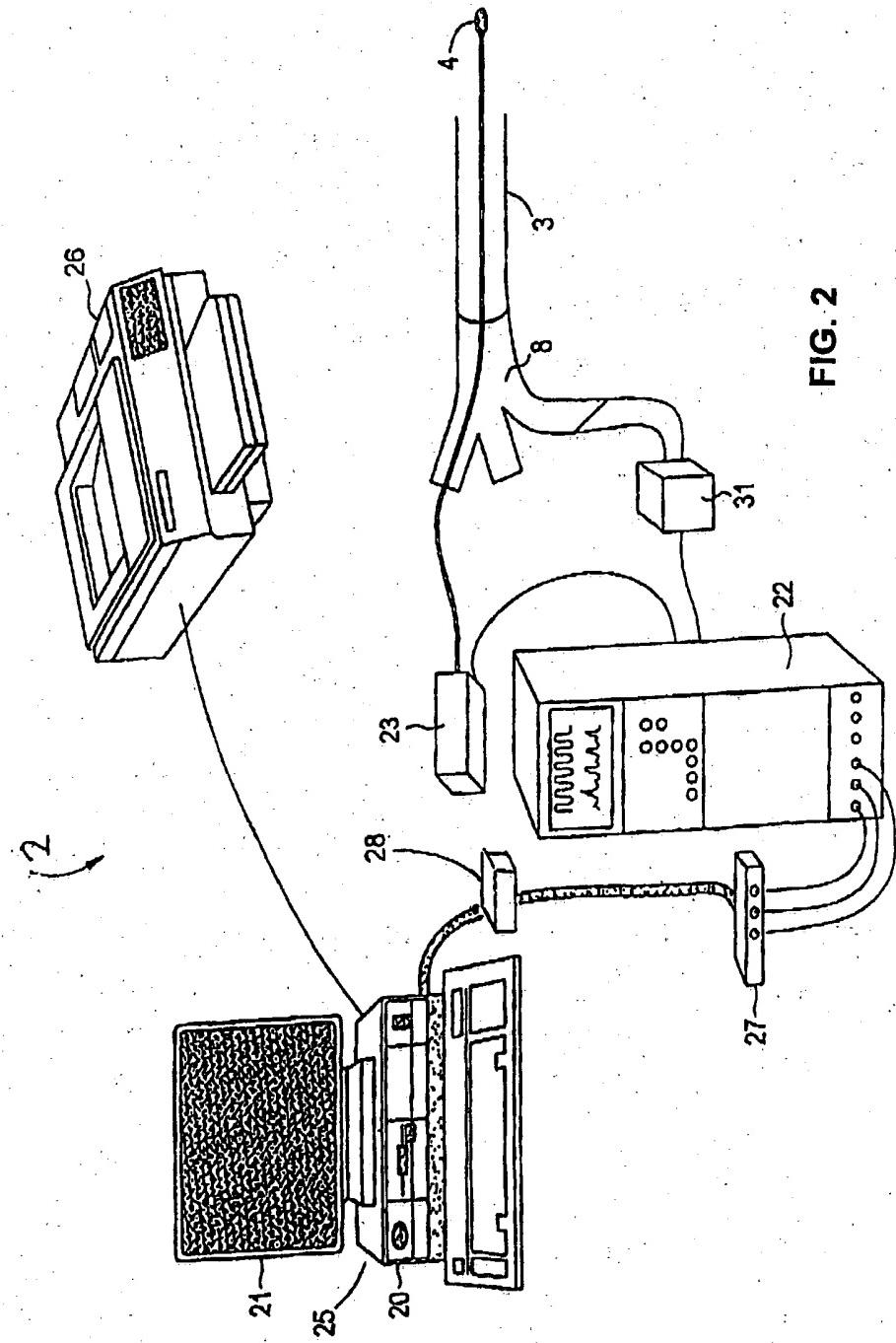


FIG. 1

2/17



3/17

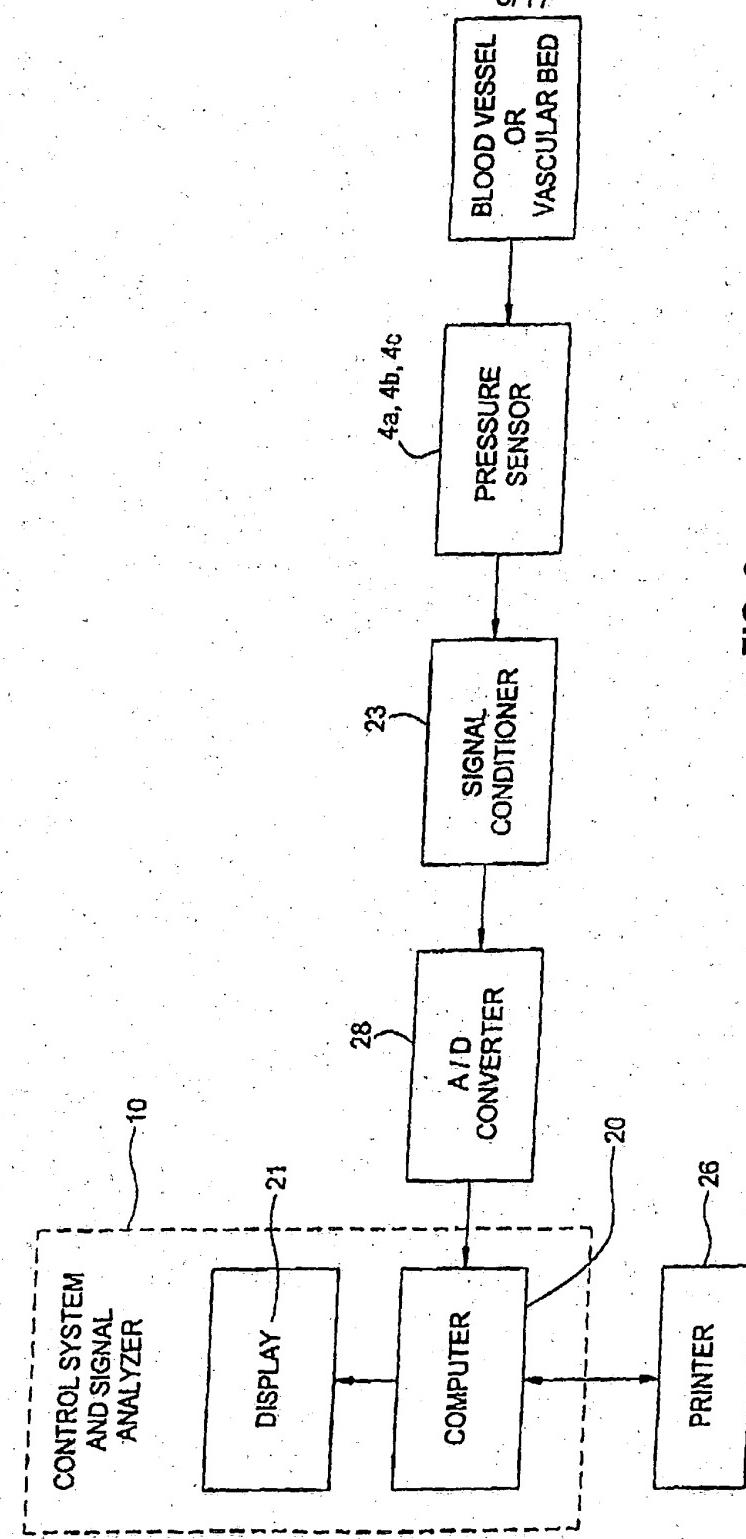


FIG. 3

4/17

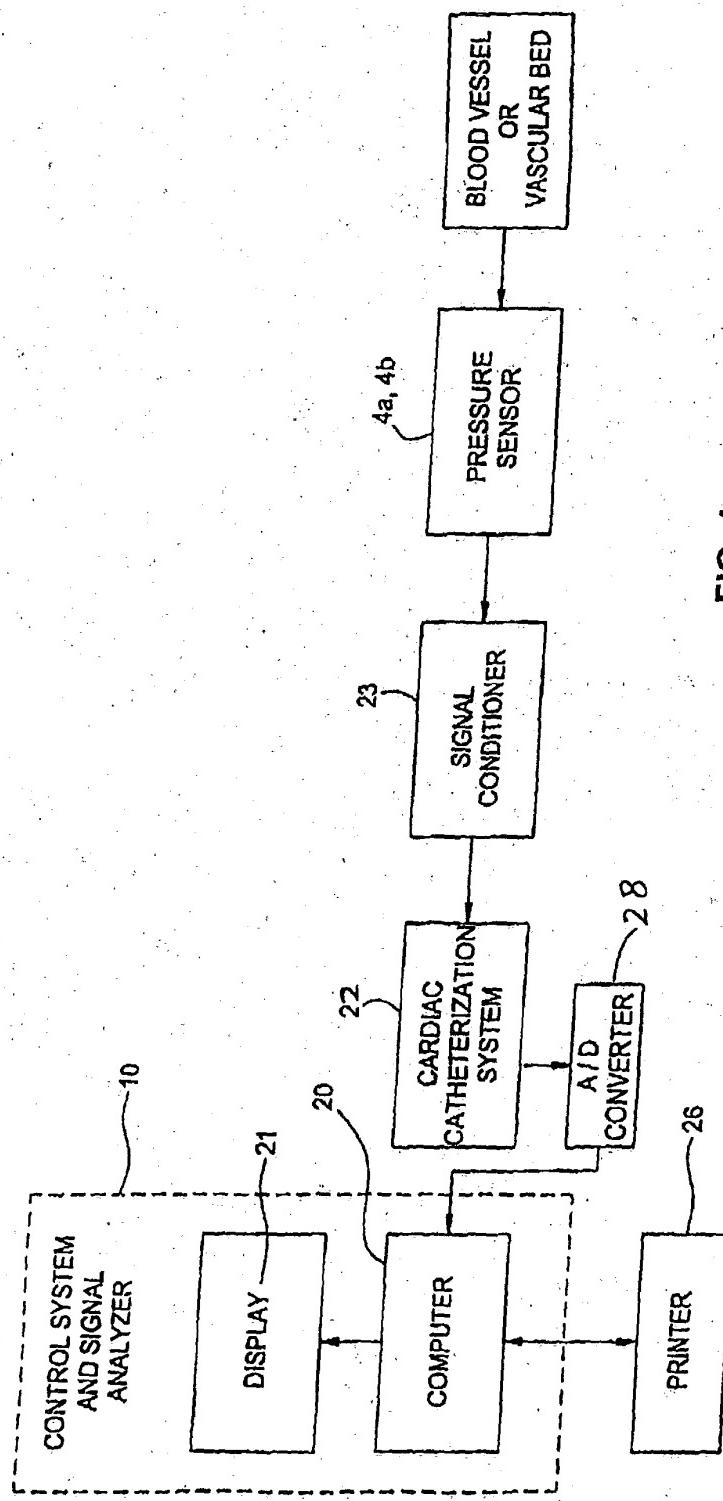


FIG. 4

5/17

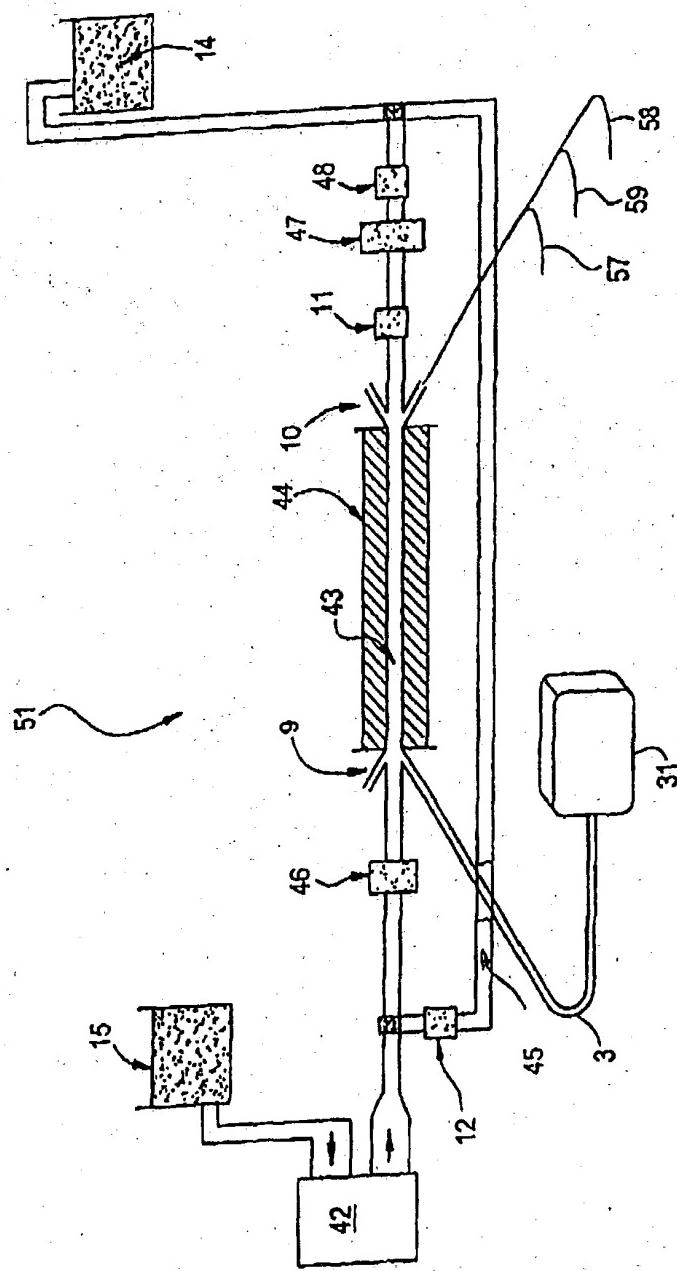


FIG. 5

6/17

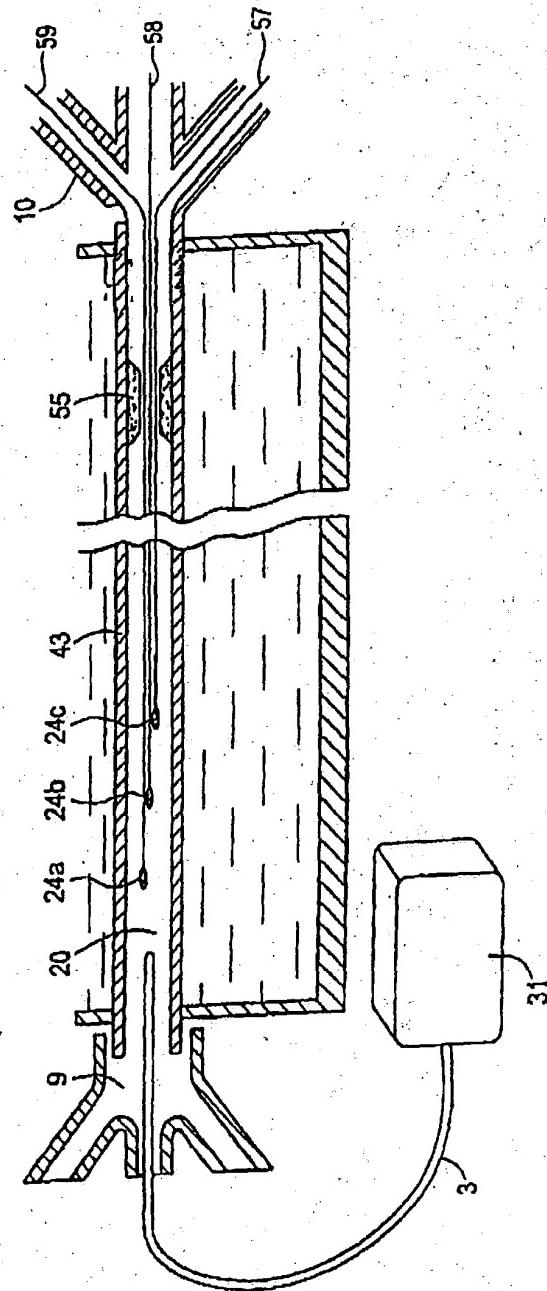


FIG. 6

7/17

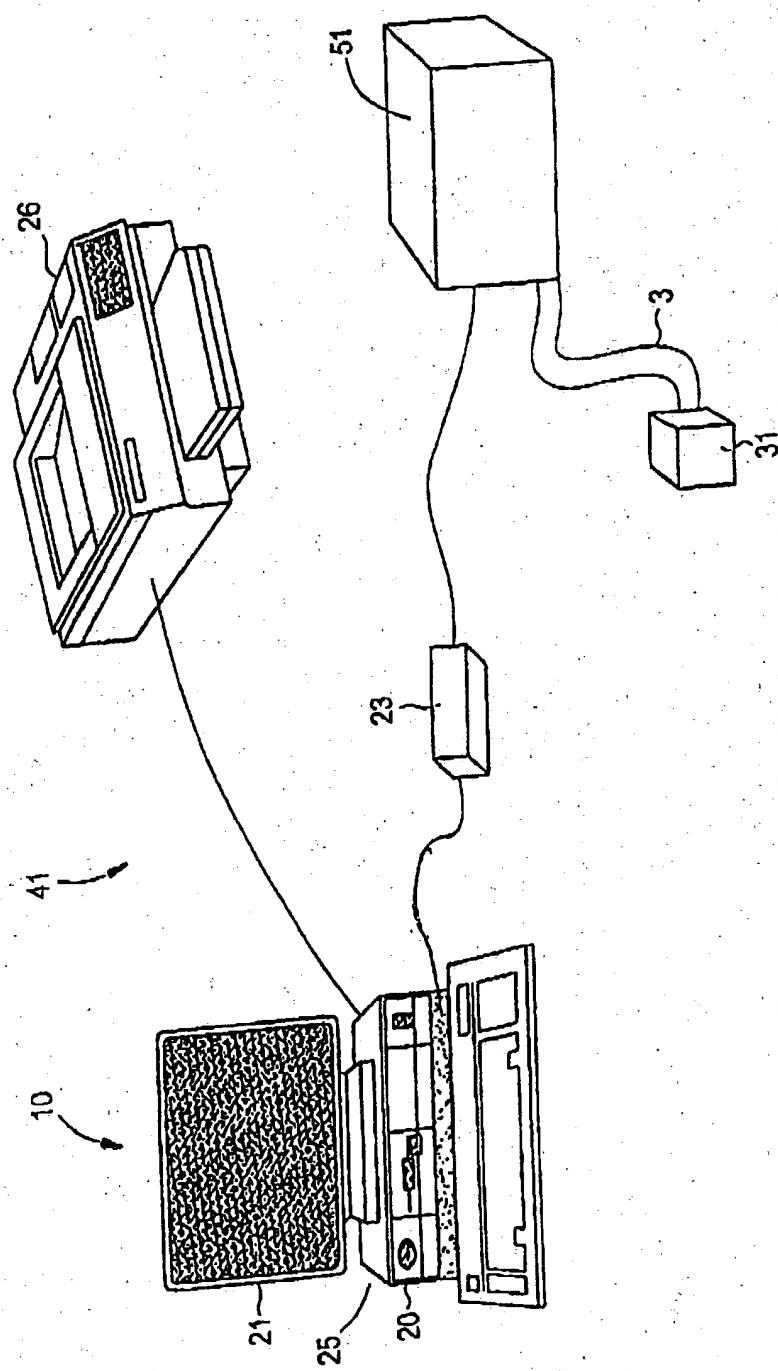


FIG. 7

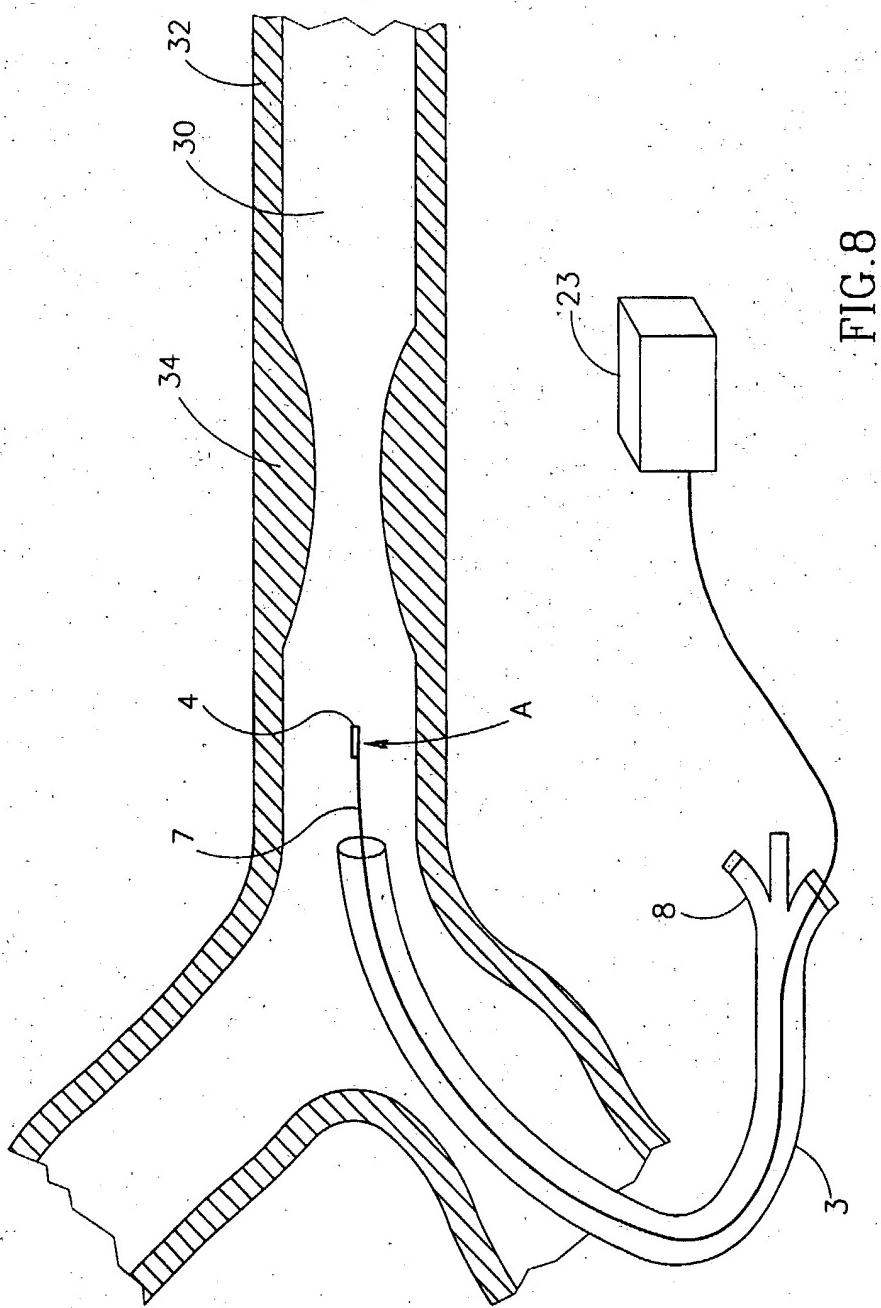


FIG. 8

9/17.

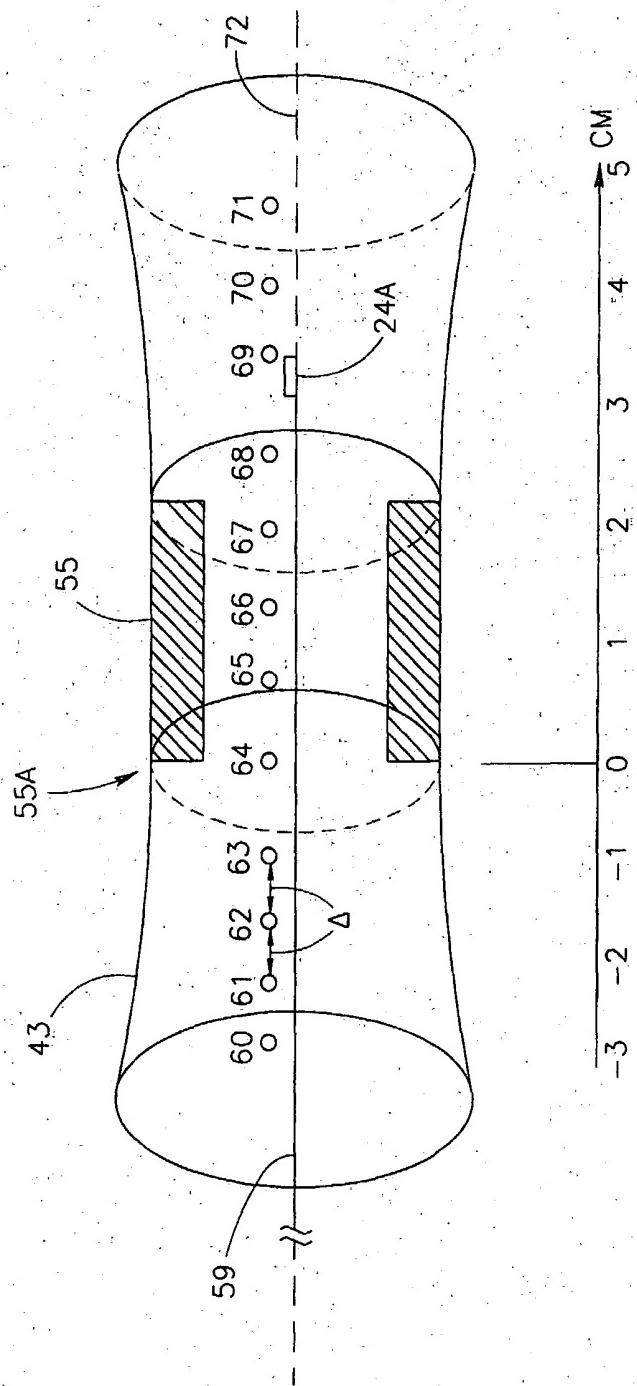


FIG.9

10/17

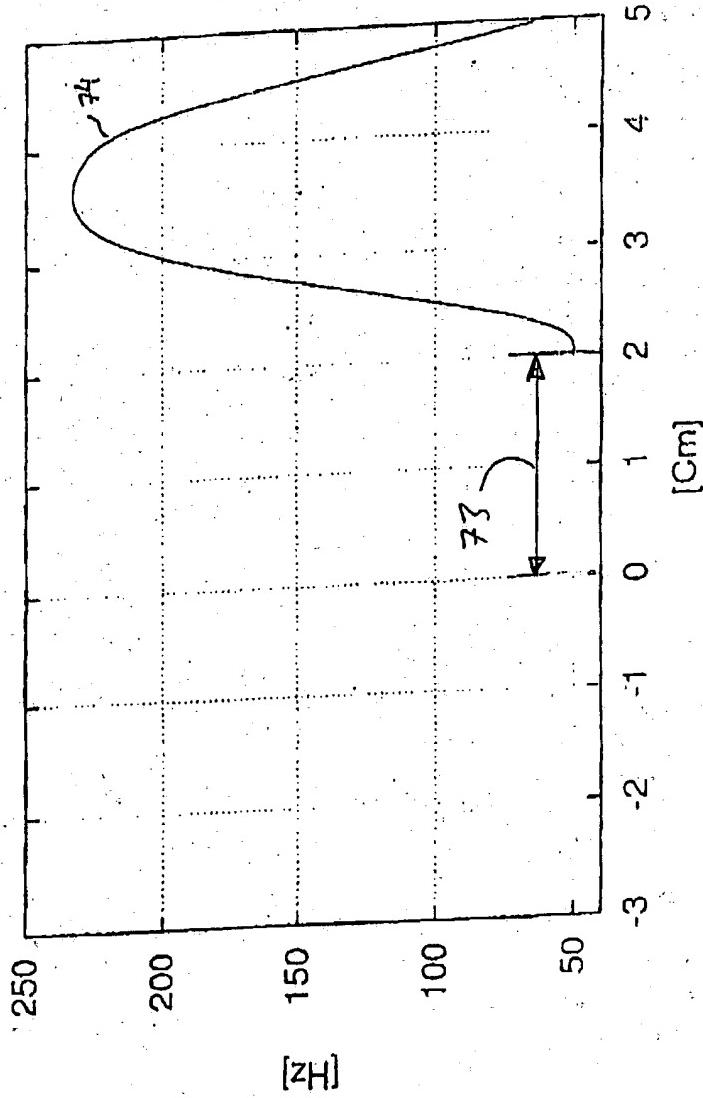


FIG. 10

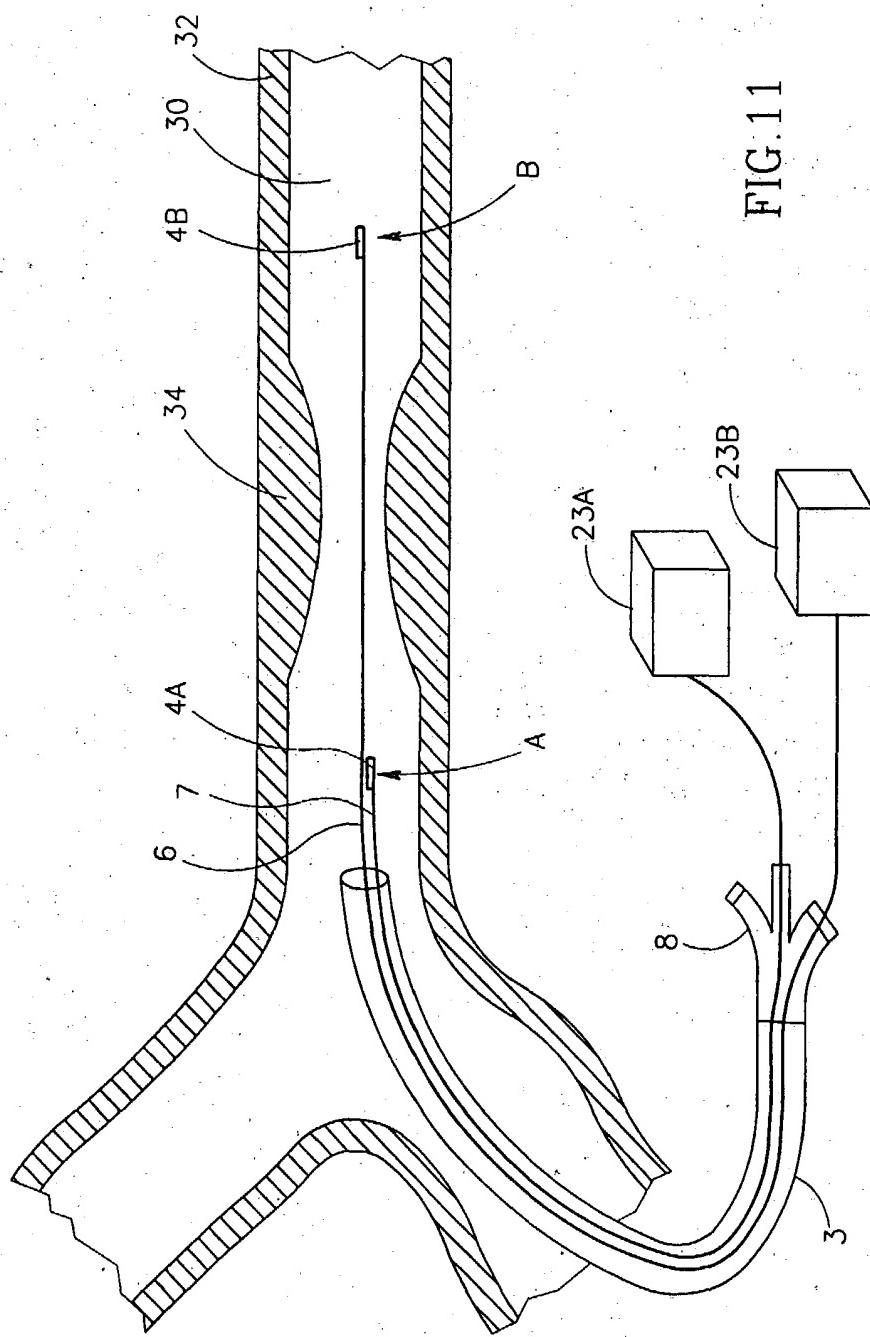
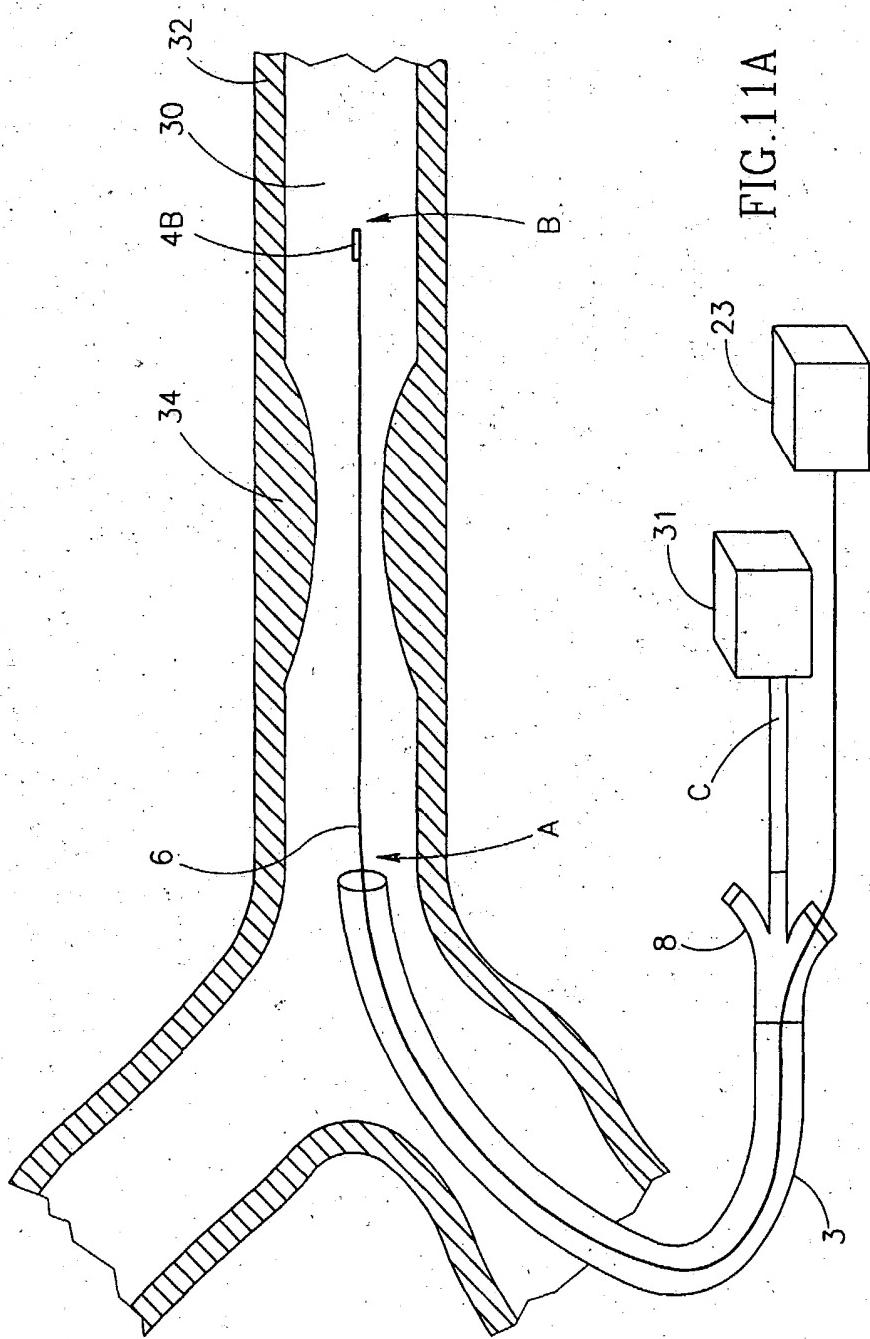


FIG. 11



13/17

FIG.12

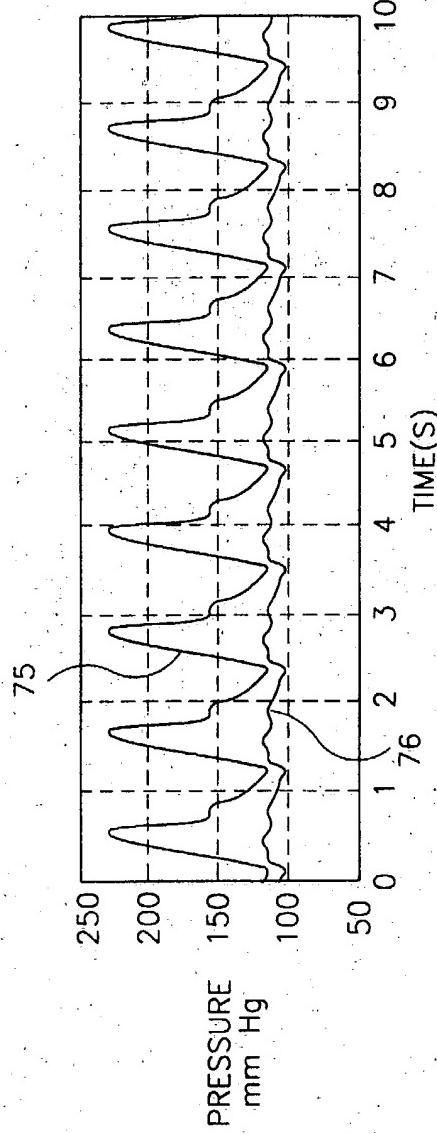
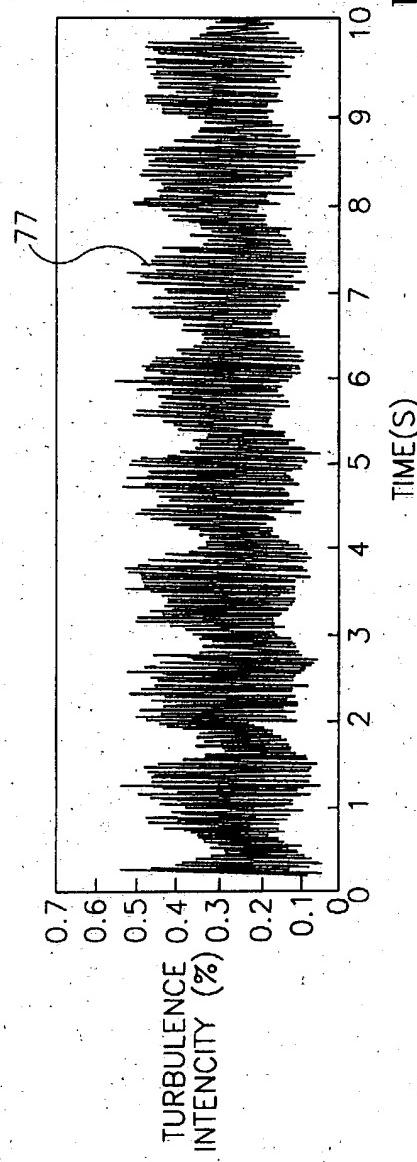


FIG.13



14/17

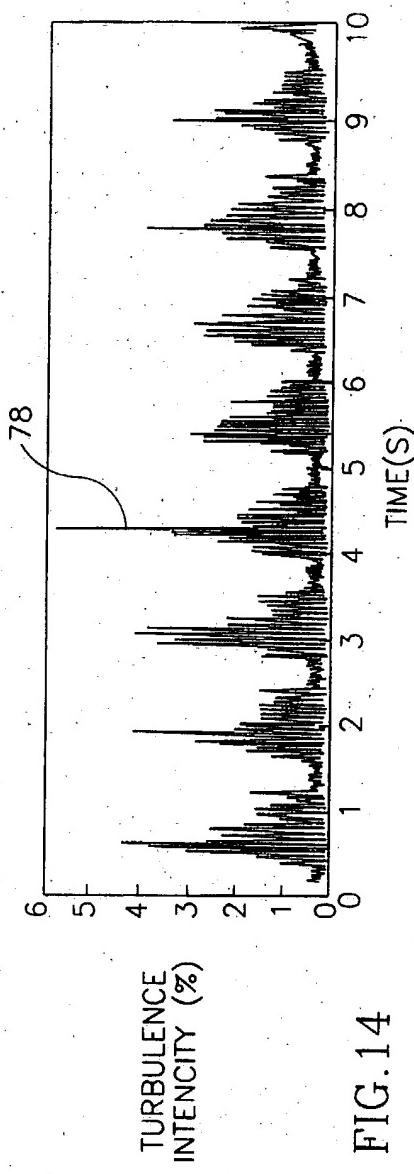


FIG. 14

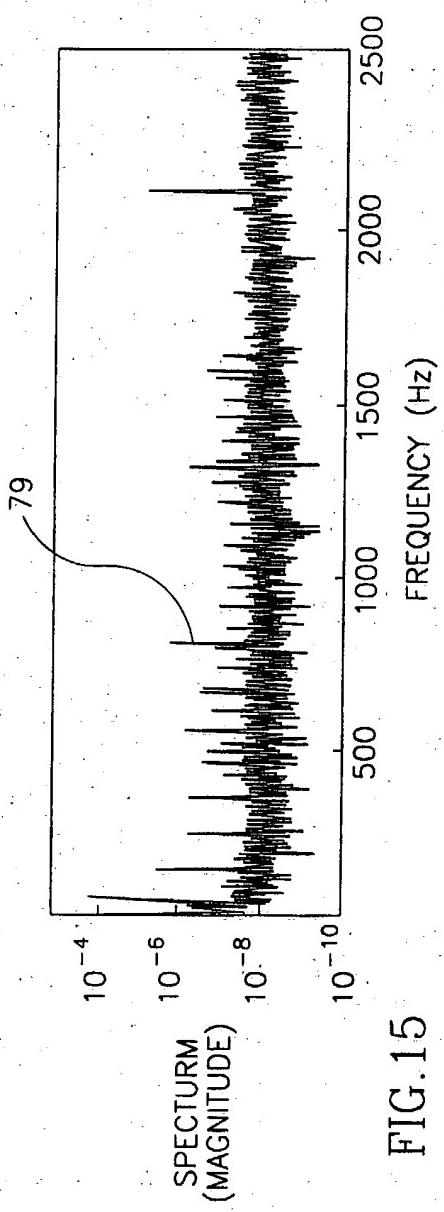


FIG. 15

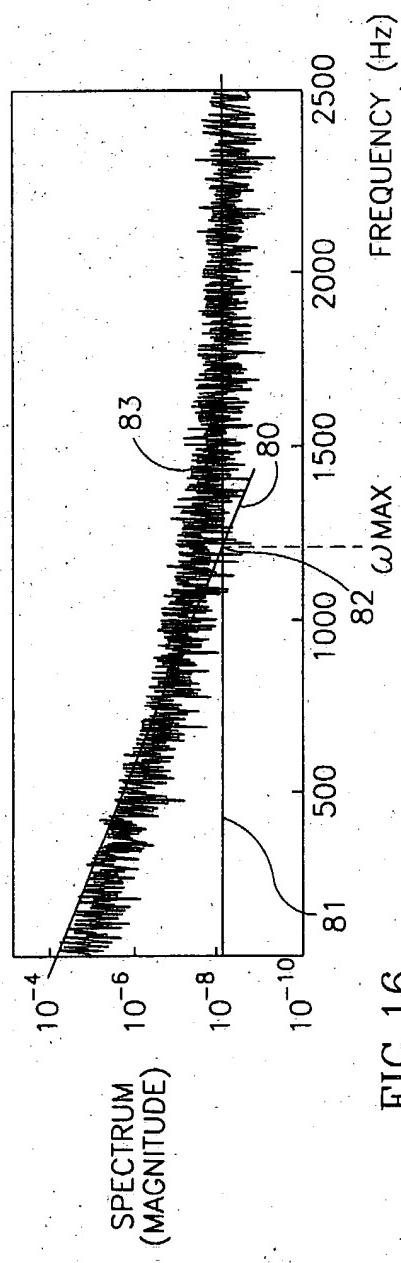


FIG. 16

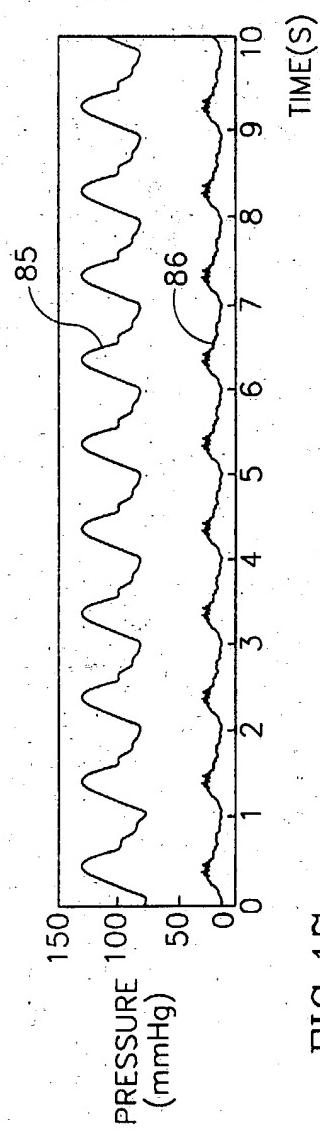


FIG. 17

16/17

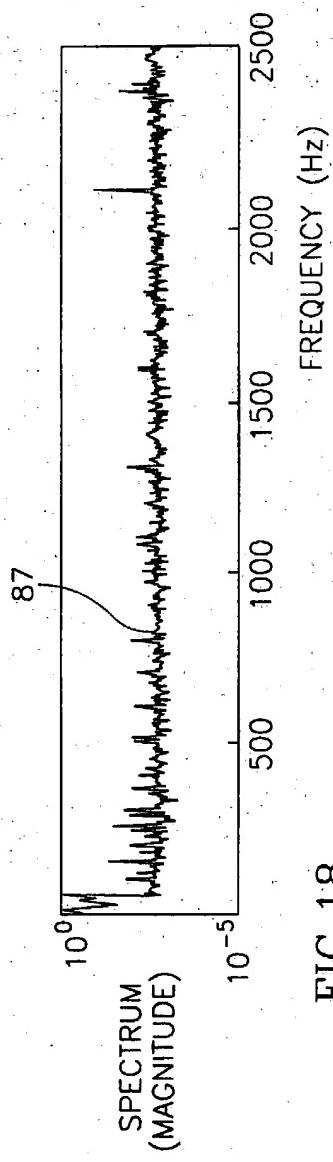


FIG. 18

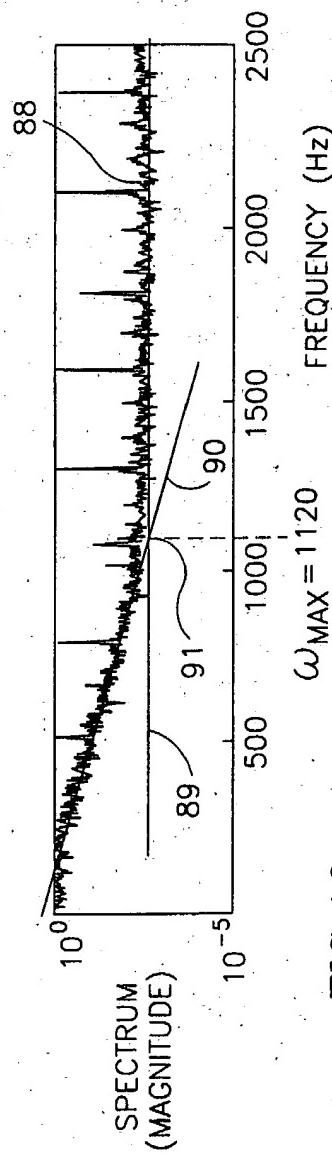


FIG. 19

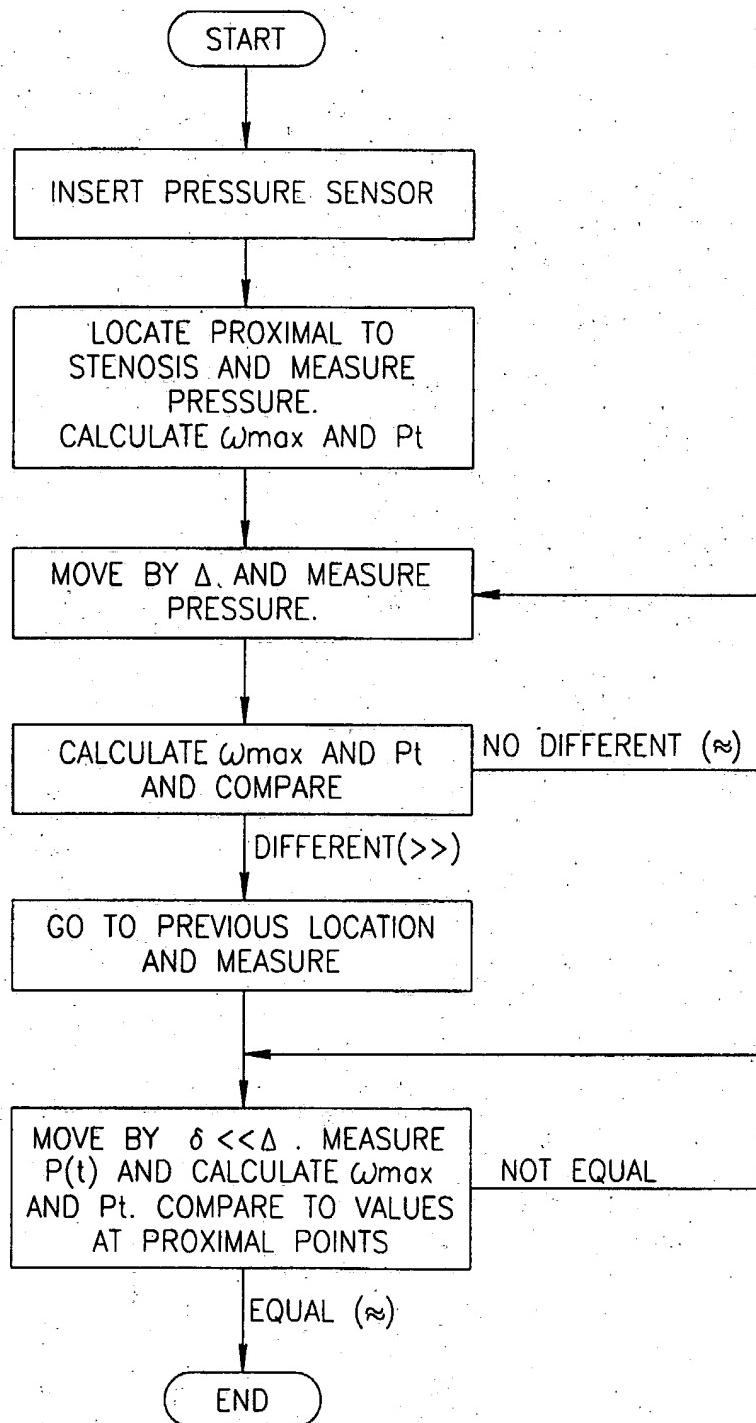


FIG.20

## INTERNATIONAL SEARCH REPORT

International application No.
PCT/IL99/00233

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) : A61B 05/00;

US CL : 600/504;

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 600/504-507, 561;

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

none

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

none

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5,178,153, A (EINZIG) 12 January 1993, entire document.	1-36

<input type="checkbox"/>	Further documents are listed in the continuation of Box C.	<input type="checkbox"/>	See patent family annex.
"A"	Special categories of cited documents: document defining the general state of the art which is not considered to be of particular relevance	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"E"	earlier document published on or after the international filing date	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O"	document referring to an oral disclosure, use, exhibition or other means	"&"	document member of the same patent family
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search  31 AUGUST 1999	Date of mailing of the international search report  28 SEP 1999
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	Authorized Officer  ROBERT L. NASSER JR.  Telephone No. (703) 308-3230
Facsimile No. (703) 305-3230	